Subliminally Presented Stimuli Modify Memory Performance

Implications for Theories of Long-Term-Memory

Dissertation

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to Jakob Lindenmeyer
and to my parents

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Original article included in doctoral thesis

A1 **Degonda, N.**, Mondadori, C. R. A., Bosshardt, S., Schmidt, C. F., Bösiger, P., Nitsch, R. M., Hock, C., Henke, K. (*Submitted*). Implicit associative learning engages the hippocampus and interacts with explicit associative learning.

Own contributions

The above mentioned manuscript is included in my written thesis as separate chapter. As a Ph.D. student I planned, designed, and carried out two of the three fMRI experiments (experiment 1 – incongruent, and experiment 2 – congruent), and the behavioural control experiment, collected the behavioural and the functional magnetic resonance imaging data, evaluated the behavioural and imaging data, wrote the first draft of the included manuscript and revised it (and later versions) after corrections of my supervisor Katharina Henke and remarks of unknown reviewers. An additional third fMRI experiment (experiment 3 – identical) was included later in the manuscript. Christian Mondadori collected and evaluated the fMRI and the behavioural data of this experiment.

The fMRI data was collected at the Institute for Biomedical Engineering (IBT) of the University and ETH Zurich together with Conny F. Schmidt and Thomas Järmann who operated the 3 Tesla Scanner when we started the data collection. Conny F. Schmidt introduced me in how to operate the 3 Tesla Scanner and supervised the further data collection.

Simone Bosshardt discussed the design and the results with me. Together, we learned how to use SPM and PMOD, the two software-tools we employed to evaluate the imaging data.

All work was done under the supervision of Katharina Henke.

Other original articles

A2 Bosshardt, S., Schmidt, C. F., Jaermann, T., **Degonda, N.**, Boesiger, P., Nitsch, R. M., Hock, C., and Henke K. *(in press).* Effects of memory consolidation on human hippocampal activity during retrieval.

A3 Bosshardt, S., **Degonda, N.**, Schmidt, C. F., Boesiger, P., Nitsch, R. M., Hock, C., and Henke, K. *(Manuscript in preparation)* One month of memory consolidation enhances retrieval-related hippocampal activity.

A4 Schmidt, C. F., **Degonda, N.,** Luechinger R. C., Henke K., Boesiger P. *(Submitted)* Sensitivity-Encoded (SENSE) Echo Planar fMRI at 3T for measurement of the Medial Temporal Lobe.

A5 **Degonda, N.**, Schmidt, C. F., Bosshardt, S., Bösiger, P., Nitsch, R. M., Hock, C., Henke, K.. (*Manuscript in preparation*). Subliminal Stimuli Improve Explicit Learning in Poor Learners.

A6 Wollmer, M. A., Papassotiropoulus, A., Streffer, J. F., Grimaldi, L. M. E., Kapaki, E., Salani, G. Paraskevas, G. P., Maddalena, A., de Quervain, D., Umbricht, D., Lemke, U., Bosshardt, S., **Degonda, N.**, Henke, K., Hegi, T., Jung, H. H., Pasch, T., Hock, C., Nitsch, R. M. (2002). Genetic polymorphisms and cerebrospinal fluid levels of tissue inhibitor of metalloproteinases 1 in sporadic Alzheimer's disease. Psychiatric Genetics, 12 (3): 155-160.

Contributions to meetings

Talks

Ph.D. Retreat Valens, May 2001

Degonda, N. Cross-talk between nonconscious and conscious memory (talk; presentation of the Ph.D. project)

Meeting of the Society for Neuroscience, Orlando, FL, USA, November 2002

Degonda, N. M., Schmidt, C., Jaermann, T., Boesiger, P., Nitsch. R. M., Hock, C., Henke, K. Nonconscious impacts conscious semantic associative encoding by way of the hippocampus. Program no. 620.3 (2002) Abstract Viewer/Itinerary Planer. Washington, DC: Society for neuroscience; [online]

Posters

ZNZ Annual Meeting, October 2002 (poster)

Degonda, N., Schmidt, C.F., Jaermann, T., Bosshardt, S., Boesiger, P., Nakkas, C., Nitsch, R. M., Hock, C., Henke, K. Invisible stimuli impact conscious learning. (Poster).

ZNZ Annual Meeting 2003 (poster)

Degonda, N., Bosshardt, S., Schmidt, C. F., Boesiger, P., Nitsch, R. M., Hock, C., Henke, K. Nonconscious Learning Modifies Conscious Learning by Way of the Medial Temporal Lobe.

Abbreviations

AP	action potentials
BOLD	blood oxygen level dependent
DNMS	delayed non-matching to sample
fMRI	functional magnetic resonance imaging
LFP	local field potentials
LOP	levels of processing
MRI	magnetic resonance imaging
MTL	medial temporal lobe
NRT	number reduction task
PET	positron emission tomography
SPM	statistical parametric mapping
SRTT	serial reaction time task
TAP	transfer appropriate processing

Contents

1 Zusammenfassung

Ein weit verbreitetes Modell für Lanzeit-Gedächtnis unterscheidet zwischen Hippocampus-abhängigen, deklarativen und Hippocampus-unabhängigen, nondeklarativen Gedächtnisformen. Das deklarative Gedächtnis umfasst willentlich abrufbare Gedächtnisinhalte und kann durch explizite Tests geprüft werden, bei denen auf die vorangegangene Lernepisode Bezug genommen wird (z.B. eine Wortliste lernen und diese später abrufen). Das nondeklarative Gedächtnis umfasst Gedächtnisinhalte, die unabhängig sind von der expliziten Erinnerung an die Lernphase, und die durch implizite Tests geprüft werden, bei denen nicht auf die vorangegangene Lernepisode Bezug genommen wird (z.B. Lernen von motorischen oder kognitiven Fertigkeiten).

"Processing" Ansätze bieten eine Alternative zu Modellen, die zwischen verschiedenen Gedächtnissystemen unterscheiden, wie z.B. das deklarative/nondeklarative Modell. In *"processing"* Ansätzen werden Lernprozesse als Verarbeitungsprozesse konzeptualisiert, die der Wahrnehmung und dem Erfassen der Bedeutung eines Ereignisses zugrunde liegen. Erinnern wird als logische Konsequenz des Lernens aufgefasst, d.h. als logische Folge der Verarbeitung eines Ereignisses.

In früheren Studien haben wir gezeigt, dass neue semantische Assoziationen zwischen Gesichtern und Wörtern mittels Hippocampus auch implizit gebildet und erinnert werden können. Basierend auf der Annahme, dass der Hippocampus involviert ist sobald semantische Assoziationen gebildet werden sollen – unabhängig davon, ob wir uns dessen gewahr werden oder nicht – haben wir die Hypothese aufgestellt, dass implizites und explizites Lernen interagieren, und dass der Hippocampus Teil des neuronalen Netzwerks ist, über welches diese Interaktionen ablaufen. In der Studie, die hier vorgestellt wird, haben wir geprüft, wie implizites Lernen von subliminal präsentierten Gesichts-Berufs-Kombinationen mit dem nachfolgenden expliziten Lernen von semantisch kongruenten oder inkongruenten supraliminal präsentierten Gesichts-Berufs-Kombinationen interagiert. Implizites Lernen von semantischen Assoziationen hat das nachfolgende explizite Lernen von semantisch kongruenten sowie semantisch inkongruenten Assoziationen beeinflusst und die spätere Abrufleistung vermindert, unabhängig davon, ob die subliminal präsentierten Gesichts-Berufs-Kombinationen inkongruent oder kongruent waren zu den Kombinationen, die explizit gelernt werden sollten. Diese Interaktion wurde über den Hippocampus und temporo-frontale kortikale Areale vermittelt.

Die beschriebenen Ergebnisse stellen somit die Kernannahme die der Unterscheidung zwischen deklarativen und nondeklarativen Gedächtnisformen zugrunde liegt in Frage, nämlich die Annahme, dass medio-temporale Strukturen ausschliesslich für explizite Gedächtnistests relevant sind. Zusätzlich haben verschiedene Autoren weitere neuere Befunde berichtet, die darauf hinweisen, dass der Hippocampus involviert ist, wann immer neue, flexible, semantische, räumlich-zeitliche und kontextuelle Verknüpfungen gebildet oder erinnert werden, unabhängig davon, ob dies implizit oder explizit geschieht.

Deshalb scheint es an der Zeit zu sein, Modelle die zwischen deklarativen und nondeklarativen Gedächtnisformen unterscheiden durch ein neues Modell zu ersetzen, welches den aktuellen Wissenstand bezüglich der verschiedenen Aspekte des Langzeit-Gedächtnisses besser erklären kann. Ein alternatives Modell für das Langzeit-Gedächtnis, welches Aspekte von "processing-" und System-Ansätzen (wie z.B. der deklarativ/non-deklarativ Ansatz) integriert wird vorgeschlagen.

2 Summary

A widely accepted model for long-term memory differentiates between hippocampus-dependent declarative and hippocampus-independent nondeclarative forms of memory. Declarative memory is accessible to conscious awareness and is usually tested with explicit memory tasks where reference is made to the previous learning episode such as learning a list of words and recalling the words later. Nondeclarative memory is independent of conscious awareness for the learning episode and is generally tested with implicit memory tasks where no reference is made to previous learning episodes such as learning motor or cognitive skills.

Processing accounts offer an alternative to the declarative/nondeclarative and other accounts segregating between different memory systems. In processing accounts memory-encoding is conceptualised as the processes underlying perception and comprehension of an event and retrieval is the logical consequence of encoding, i.e. processing and event to perceive and understand it.

In previous studies we have shown that new semantic associations between faces and words can be formed and retrieved by way of the medial temporal lobe (MTL) without awareness. Based on the assumption that the hippocampus is engaged in establishing new semantic associations between faces and words with and without conscious awareness, we hypothesised, that implicit and explicit learning would interact and that interactions would be mediated by a network including the hippocampus. In the study presented in this doctoral thesis we tested for interactions between the implicit learning of subliminally presented face-profession pairs and the subsequent explicit learning of either semantically congruent or incongruent supraliminal face-profession pairs. We found that implicit semantic associative learning modified later explicit semantic associative learning of both congruent and incongruent item pairs and that later explicit retrieval performance was reduced irrespective of whether explicit learning had been preceded by the subliminal presentation of incongruent or congruent face-profession pairs. This interaction was mediated by the hippocampus and temporal-frontal cortices. Our design allowed us to conclude that the implicit representations demonstrated a compositionality and flexibility which had previously been attributed to explicit memories alone.

Thus, the findings reported in the present study heavily challenge the central claim of the declarative/nondeclarative account suggesting that MTL structures are exclusively involved in declarative memory or explicit tasks. Recent findings reported by several authors provide increasing evidence that the hippocampus is involved in the formation and recollection of new, flexible, semantic, spatial-temporal and contextual relations, irrespective of the level of awareness involved at learning or retrieval.

Therefore, it might be time to abandon declarative/nondeclarative accounts in favour of a model for long term memory that provides better explanation for the current status of knowledge about different aspects of long term memory. An alternative model for long-term memory will be suggested in this doctoral thesis, integrating aspects of processing accounts and systems (e.g. declarative/nondeclarative) accounts.

3 Theoretical background – Long term memory is not a unitary system

3.1 Discovering the neural substrates of long-term memory

3.1.1 Learning from amnesic patients

The first major breakthrough in understanding the neural substrates of long-term memory came with Scoville and Milner's (1957) report of severe and persistent memory deficits after bilateral resections of the medial temporal lobes (MTL, see Figure 1). Their report made clear that MTL structures are of crucial importance for long-term memory. They assessed performance in formal memory and intelligence tests in ten patients (eight psychotic patients, one patient with intractable epileptic seizures, and one patient with incisural herniation) with similar bilateral MTL resections that extended for varying distances along the mesial surface of the temporal lobes. All patients with a resection that damaged portions of the hippocampus and the hippocampal gyrus bilaterally, did show a persistent disturbance of memory. This led the authors to the conclusion that the anterior hippocampus and the hippocampal gyrus, either separately or together are of crucial importance for the retention of current experience. In the two most radical resections that destroyed presumably the anterior two-thirds of the hippocampus and hippocampal gyrus, as well as the uncus and amygdala, a complete loss of memory for events was observed.

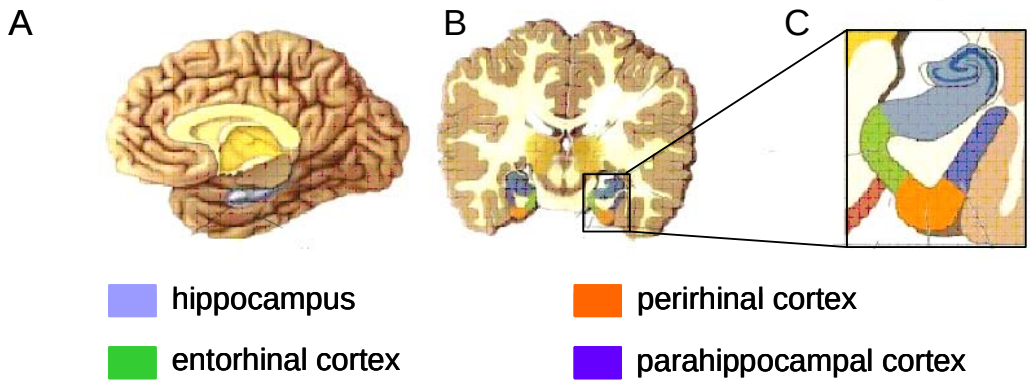

Figure 1. Sagittal (A) and coronal (B) view of medial temporal lobe (MTL) structures, especially the hippocampal formation. The detailed view (C) shows the subdivision in hippocampus, entorhinal cortex, perirhinal cortex and parahippocampal cortex. (Taken from the internet: http://www.physiology.wisc.edu/neuro524/learningI02/Slide12.jpg)

The severe memory impairment contrasted sharply with the preserved motor, perceptual, language and attentional abilities and the good general intelligence of these two patients. The patients appeared to forget events as fast as they happen and to be unable to acquire new information, i.e. they showed a severe anterograde amnesia. In addition, they showed a graded retrograde amnesia, i.e. they showed a memory loss for past events that was most severe for events that happened just prior to the operation, whereas memory for remote events was spared (Figure 2).

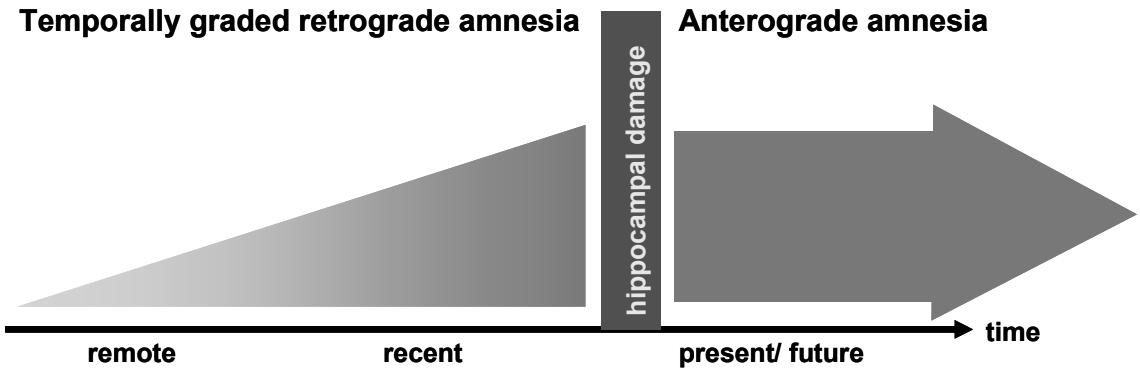

Figure 2. Hippocampal damage leads to severe anterograde amnesia as well as to temporally graded retrograde amnesia.

One of these two patients with the most radical resections was H.M. who was operated for release from severe epileptic seizures and whose case is reported in almost every text book about long-term memory today. A careful reinvestigation of H.M. revealed that the inability to acquire new information was not complete. Corkin (1968) observed that he was able to learn new motor skills, although he was severely impaired in a wide variety of memory tasks, including free recall of short prose passages and complex patterns, face recognition, continuous recognition of visual patterns and of verbal material, paired-associate learning, and maze learning. She concluded from these results that motor learning is not dependent from MTL structures and more importantly that more than one set of neural structures is concerned with long-term memory, i.e. long-term memory seemed not to be a unitary system that is subserved by MTL structures.

A further major step in understanding long-term memory was reached in the eighties, when Cohen and Squire (1980) elucidated more specifically which type of learning was spared in amnesic patients. They demonstrated that amnesic patients successfully can acquire a mirror reading skill and concluded from this observation that the class of preserved learning skills in amnesic patients is not limited to perceptuo-motor skills. They hypothesised that there is rather a distinction between "knowing how", i.e. memory for procedural or rule-based information (classically tested with the acquisition of perceptuo-motor skills or mirror reading), and "knowing that", i.e. memory for declarative or data-based information (classically tested with recall and recognition tasks) and that different neural substrates underlie the two different types of memory.

Since the initial observation of preserved ability to acquire new perceptuomotor skills in H.M., the range of tasks in which amnesic patients show normal performance has been substantially enlarged. The capacity for nondeclarative learning is now also assessed using tasks such as probabilistic classification learning, artificial grammar learning, word and picture priming, as well as conditioning tasks (Gabrieli, 1998; Schacter et al., 1993; Squire, 1992a; 1992b; Squire et al., 1993) for reviews.

3.1.2 Simulating amnesia in animals

It was not only the investigation of amnesic patients that has revealed how long-term might be organised in the brain. Important evidence came also from experiments with animals, above all with rats and monkeys. Efforts to develop animal models for amnesia following MTL damage in rats and monkeys started as soon as the case of H.M. was published (for a review see Eichenbaum, 2002b). A valid animal model should mirror as closely as possible the syndrome as it is observed in human patients. Therefore, an animal model of the human amnesic syndrome should exhibit the following characteristics: 1) intact sensory, motor, motivational, attention and cognitive processes, 2) intact short-term memory, 3) long-term memory declines with abnormal rapidity, i.e. much faster than expected for normal forgetting, 4) the long-term memory deficit is not limited to one type of information, i.e. it can be observed for conceptual as well as for sensory modalities of learning, 5) graded retrograde amnesia.

The first step in developing a model for the human amnesic syndrome in monkeys was to reproduce the lesions that led to the amnesic syndrome in humans. The second step was to find a task that revealed memory deficits in the lesioned monkeys of comparable severity to the deficits that were observed in humans. This goal was obtained with the delayed non-matching to sample (DNMS) task, a task that revealed severe memory deficits in monkeys with MTL lesions (Mishkin, 1982). The key aspect of this task compared to previously used tasks that revealed only relatively mild memory deficits in the lesioned monkeys, is the "trial-unique stimulus" procedure. This means that each stimulus is used only in one trial. In each trial of the DNMS monkeys are presented with an object and removing the object is rewarded with food. After a delay, the monkey is presented with the same and a novel object, whereas this time, reaching for the novel object is rewarded with food. Because every stimulus is presented only in one trial, the monkeys have to learn the general rule, i.e. that they have to reach for the novel object in each trial.

It was not easy to find tasks in which rats with hippocampal damage failed to show normal performance. Astonishingly, rats with hippocampal lesions even outperformed controls in some of the used simple conditioning and discrimination learning tasks (e.g. Eichenbaum et al., 1988). The breakthrough in animal models for rats was achieved with the observation that rats with hippocampal lesions had a selective impairment in spatial learning. Currently, two spatial memory tasks have received wide-spread use: the Morris water maze task, developed by Morris (1982) and the radial-arm maze as used for example by Olton and colleagues (1979). The Morris water maze consists of a large, round swimming pool that is filled with water (see Figure 3). A platform is hidden at an arbitrary place just beneath the surface. Milk powder is added to the water, to make it opaque, so that the platform is not visible.

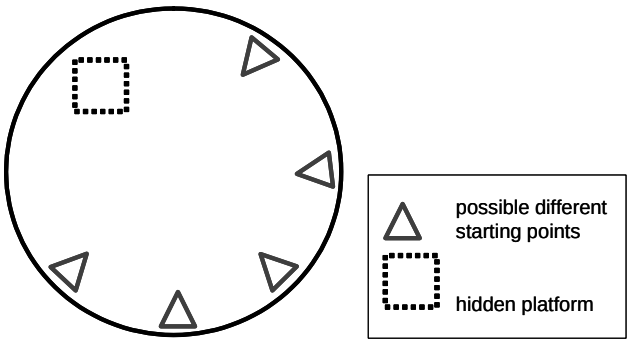

Figure 3. An overhead view of the Morris water maze.

Rats are good swimmers, but they prefer not to swim and are therefore highly motivated to find the platform and climb onto it, to escape the water. Because they can not see directly the platform, they have to use distant spatial cues to navigate to the hidden platform. In the standard task the rats have to navigate to the hidden platform starting at multiple different locations. Therefore they have to combine the experience they made in the different trials and to construct a cognitive map reflecting the relations among distant spatial cues. In a subsequent "transfer test" the platform is removed and the rats are allowed to swim for 1 minute in the water maze. The measure for memory is the time the rats spend in the quadrant of the pool where the platform had been in the previous trials. Normal rats have a strong tendency to swim in the close vicinity of the place where the platform had been and therefore spend a lot of time in this quadrant. In contrast, rats with hippocampal lesions show no preference for this quadrant, indicating that they had not been able to learn and to remember the location of the platform. However, rats with hippocampal lesions succeed in a variant of the classical version of the water maze task where they start always from the same starting point during the training phase (summarised in Eichenbaum, 2002b).

The radial-arm maze typically is composed of eight runway arms radiating outward from a central platform (see Figure 4). There are many variants of the number of arms and of reward contingencies, such as rewarding every arm just once or rewarding a certain number of arms just once. On the standard variant a reward is placed at the end of each arm and the reward is not replaced during this trial. The rat is free to enter the different arms and learns fast to enter each arm just once. The number of arms a rat entered is used as a measure for the ability to remember which arms it already had visited on this particular trial.

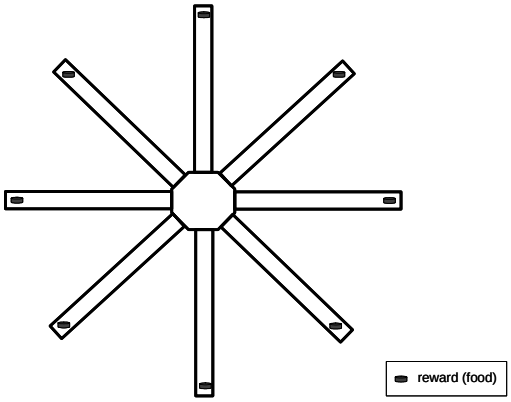

Figure 4. An overhead view of a typical radial arm maze with eight arms.

The experiments in animals have provided further support for the hypothesis that memory is not a unitary system but consists of different subsystems depending on different, though overlapping neural networks (Eichenbaum, 2002b; Eichenbaum, 1997; Milner et al., 1998; Squire, 1992b; Squire, 1992a; Squire and Zola, 1996; Squire and Zola-Morgan, 1988).

Experimentally induced lesions allow studying the role of MTL structures in animals

An advantage of experimentally induced lesions is that the extent of the lesion can be controlled fairly well. Therefore, studies with lesioned animals have provided important evidence concerning the role of different MTL structures. Different roles in long term memory processes are for example suggested for the perirhinal cortex and the hippocampus. Evidence implies that the perirhinal cortex is crucially involved in familiarity based recognition processes and learning of single items, whereas the hippocampus is supposed to be critically engaged in recollection of events and learning of spatial and non-spatial relations or associations (Aggleton and Brown, 1999; Brown and Aggleton, 2001).

Evidence for distinctive roles of perirhinal cortex and hippocampus in humans

Davachi and colleagues (2003) have recently provided additional support for distinctive roles of perirhinal cortex and hippocampus in long-term memory processes with an elegant event-related fMRI study in humans. Across fMRI encoding scans participants encoded visually presented 200 adjectives with two different encoding tasks, i.e. an "Image" task, and a "Read" task. During "Image" trials participants generated a mental image of a spatial scene described by the adjective (e.g. for "dirty" they might imagine a garbage dump). During "Read" trials participants covertly pronounced the word backwards. After a delay of about 20 hours memory for the studied words was tested in a two-step memory test. All studied words as well as 400 novel, unstudied words were presented and participants indicated for each word first whether they recognised the word as one of the studied list by responding "old" or "new". For "old" answers, they further indicated, which encoding task they performed with this word (source recollection) by responding "Image" or "Read". The answers of the recognition task were used to analyze the fMRI encoding data according to subsequent single item and source memory. Davachi and colleagues (2003) reported that encoding activation in hippocampus and posterior parahippocampal cortex predicted later source recollection but did not correlate with item recognition. In

contrast, encoding activation in perirhinal cortex predicted later item recognition, but not subsequent source recollection. They concluded from these findings that the subregions within the MTL subserve distinct, but complementary, learning mechanisms.

3.1.3 Long-term memory dissociations in normal humans

Dissociations between different types of long-term memory have also been observed in healthy adults. For example, a learning task that requires semantic judgements, such as pleasant/unpleasant will lead to higher performance in tasks where the previously learned information (often a list of words or pictures) has to be recalled or recognised compared to learning tasks requiring superficial or more perception based judgements, such as counting the number of vowels in each word (Craik and Tulving, 1975). This is the basic claim of the levels of processing approach of Craik and Lockhart (Craik and Lockhart, 1972). However, changing the modality of the presentation, such as visual versus auditory has no impact on performance in free recall or recognition tasks. In contrast, performance in visual priming tasks is not modified by manipulating the depth of processing at encoding, but depends strongly on the modality of the initial presentation at encoding. Furthermore, attentional manipulations impact performance in recall or recognition tasks but not in visual priming tasks. If participants are for example asked to read a list of words while at the same time performing a difficult secondary task, subsequent recall or recognition performance will be severely impaired relative to the case, when participants pay full attention to the study list. On the contrary, the reduced amount of attention available for encoding the words has little or no effect for the performance in priming tasks (Schacter and Buckner, 1998; Schacter et al., 1993).

Since the hypothesis that memory consists of different subsystems depending on different neural networks has arisen, there have been attempts to develop models describing the different subsystems functionally and/or neuroanatomically. A common model of long-term memory systems, aiming to distinguish different forms of memory based on distinct functional as well as neuroanatomical features will be introduced in the following section.

3.2 A common model of long-term memory systems

Cohen and Squire (Cohen and Squire, 1980) observed an impaired ability to learn and remember declarative or data-based information that contrasted with a preserved ability to learn and remember procedural or rule-based information in amnesic patients. This differentiation between impaired memory for declarative ("knowing that") and preserved memory for procedural ("knowing how") information was the basis for Squires model of long-term memory systems. After their initial observation additional forms of memory that are preserved in amnesia have been detected. The term "procedural" turned out to be too specific to summarize all forms of memory that are preserved in amnesic patients. Squire and Zola-Morgan therefore replaced "procedural" by the more neutral term "nondeclarative" in 1988 when they introduced a taxonomy of long term memory (Squire and Zola-Morgan, 1988), now differentiating between declarative and nondeclarative forms of memory (Figure 5). Declarative memory refers to the conscious recall of previous experience whereas nondeclarative memory refers to the nonconscious recollection of previous experience and is typically expressed through performance changes or training effects. Whereas declarative memory concerns recollection, nondeclarative memory concerns behavioural changes.

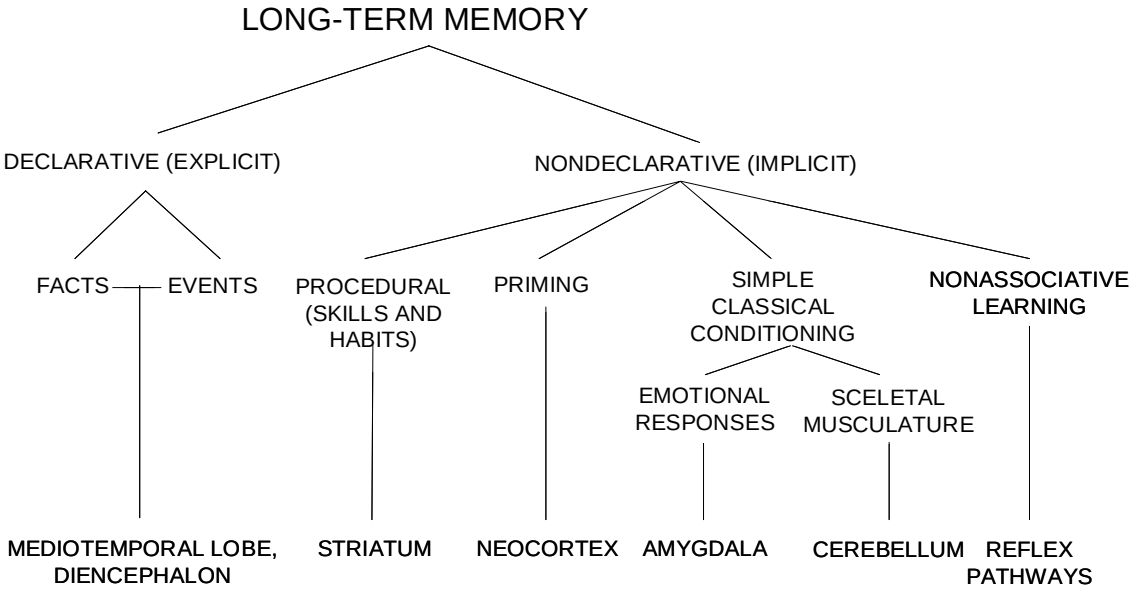

Figure 5. The organisation of declarative and nondeclarative long-term memory as proposed by Squire and Zola (1996).

3.2.1 Declarative memory

> *"Declarative memory is explicit and accessible to conscious awareness, and it includes the facts, episodes, lists, and routes of everyday life. It can be declared that is, brought to mind verbally as a proposition or nonverbally as an image."* (Squire, 1986; *p. 232*).

Declarative memory was further subdivided by Tulving (1972) into episodic memory, the memory for episodes and their temporo-spatial context, often also referred to as autobiographical memory, and semantic memory, the memory for facts. If you think about Paris, you might remember your last trip to this city in spring five years ago and how astonished you were, when you visited the Louvre and looked for the first time at the famous painting showing Mona Lisa. This is a typical example for an episodic memory, as you remember the temporo-spatial context, and your personal feelings and experiences while you looked at Mona Lisa in the Louvre in Paris. However, if you remember that Paris is the capital city of France and that the Mona Lisa is exhibited in the Louvre in Paris you retrieve facts that are stored in your semantic memory.

In experiments, declarative memory is in general studied with explicit learning tasks where the participants are presented with stimuli that they have to retrieve after a determined delay. Retrieval can be tested with free recall, i.e. participants have to retrieve the stimuli without any help, with cued recall, i.e. the first letter or syllable of previously presented words is presented as help, or with recognition tasks, where participants have to select the learned stimuli among a list consisting of the learned stimuli and a number of new distracter stimuli.

The anatomical substrates that are assumed to be necessary for declarative episodic memory are the medial temporal lobes (MTL) and the diencephalon which interact with the neocortex (Cabeza and Nyberg, 2000; Cohen and Eichenbaum, 1993; Davachi et al., 2003; Henke et al., 1997; Henke et al., 1999; Lepage et al., 2000; Mayes et al., 1998; Montaldi et al., 1998; Schacter and Buckner, 1998; Small et al., 2001; Sperling et al., 2001). The structures that are associated with declarative semantic memory are the left inferior frontal gyrus and the left lateral temporal neocortex (Cabeza and Nyberg, 2000; Martin and Chao, 2001; Pilgrim et al., 2002; Wagner et al., 2001).

3.2.2 Nondeclarative memory

In contrast to declarative memory, which appears to delineate a relatively homogeneous form of memory, nondeclarative memory refers to a rather heterogeneous collection of different learning capacities that are not dependent on conscious awareness for the learning episode or the learning material. Nondeclarative memory includes procedural memory, i.e. the acquisition of new skills and habits, the phenomenon of repetition priming as well as classical conditioning (for reviews see Gabrieli, 1998; Squire 1992; Squire et al., 1993)

Skills and habits (procedural memory)

"Skills are procedures (motor, perceptual and cognitive) for operating in the world; habits are dispositions and tendencies that are specific to a set of stimuli and that guide behaviour." (Squire et al., 1993; p. 471)

Sensorimotor and perceptual skill learning is commonly assessed with mirror tracing, rotatory pursuit and serial reaction time tasks in humans (SRTTs; Gabrieli, 1998). In mirror tracing tasks, participants trace a figure with a pen while they see their hand, the pen and the figure only reflected in a mirror. With increasing practice the number of errors and the time participants need to trace the figure decrease. In rotatory pursuit tasks participants have to maintain contact between a stylus they hold in their hand and a target on a rotating turntable. Participants can keep contact between the stylus and the target longer with increasing practice. In SRTTs participants typically see targets appear in one of four locations and have to press a corresponding button as soon as the target appears. In the critical trials the targets appear in a repeating sequence of 10-12 trials. With increasing number of repetitions of the same sequence the reaction times decrease compared to when targets appear in random sequences, although participants are unaware of the fact that a certain sequence is presented repeatedly.

Mirror reading was the first task used to investigate perceptual skill learning, i.e. over several trials participants read texts that are written in mirror letters faster. Learning of sensorimotor skills as well as perceptual skills is intact in amnesic patients, but impaired in Huntington's disease patients. Therefore, it is suggested that the basal ganglia are crucial for the learning of sensorimotor and perceptual skills. Additionally, the cerebellum and motor cortex are proposed to underlie perceptuomotor skill learning.

Cognitive skill learning refers to tasks that require planning and problem-solving such as for example tower tasks. It seems that amnesic patients are able to acquire cognitive skills normally under relatively narrow circumstances but that they are outperformed by normal participants at later stages of acquisition of more complex skills.

Different tasks, such as probabilistic classification learning, artificial grammar learning, or category learning and prototype abstraction are used to investigate kinds of learning in humans that are analogous to the habit learning tasks studied in experimental animals (Squire and Zola, 1996). In *probabilistic classification learning*, participants try to learn a set of associations that are not obvious and not reliable, due to the probabilistic structure of the task, making it difficult to memorize them. In one such task participants played the role of a weather forecaster and tried to predict from presented cues whether there will be rain or sunshine. Amnesic patients showed normal performance although they were severely impaired at remembering explicit questions about the training episode. Furthermore, they performed poor in transfer tests requiring the flexible use of the task knowledge. Patients suffering from Huntington's disease are impaired in cognitive skill and probabilistic classification learning as in sensorimotor and perceptual skill learning. The findings in amnesic and in Huntington's disease patients suggest that these forms of learning do at least to some extent depend upon the basal ganglia but not upon the medial temporal lobes.

In tasks of *artificial grammar learning*, participants are presented with a number of letter strings generated by a rule system. Participants are not told that the presented letter strings were generated by a rule system before all letter strings have been presented. Nevertheless, participants do acquire the ability to classify new letter strings as either grammatical or nongrammatical even though they are unable to articulate the nature of the rule.

Category learning and prototype abstraction tasks are very similar to artificial grammar learning tasks. Participants inspect a series of training stimuli. Afterwards, they are able to classify novel stimuli according to whether they do or do not belong into the same category as the training stimuli. Amnesic patients show normal performance in probabilistic classification tasks, normal classification performance in grammar learning as well as in category learning and prototype abstraction tasks.

However, they do not recognize the letter strings or prototypic stimuli that were presented during training, although their classification performance is normal.

Conditioning

In classical conditioning experiments studying the eye-blink response, the subjects (humans or animals) are presented with a tone (conditioned stimulus, CS), and after the tone has started (but is still present) an air puff (unconditioned stimulus UCS) is presented to the eye. The air puff initiates a reflexive eye-blink response (unconditioned response, UCR). The tone and the air puff terminate at the same point in time. After several coincident presentations of the tone and the air puff (CS-UCS combinations) the presentation of the CS alone initiates the eye blink (conditioned response, CR), i.e. the eyes are closed before the air puff starts. The memory system underlying the classical conditioned eye-blink response is very well studied (Gabrieli, 1998). The neural substrate that is assumed to be of crucial importance in classical conditioning is the cerebellum. Whereas MTL lesions do not affect classical conditioning where the presentation of the CS and the UCS overlap, conditioning is severely impaired in patients or animals with MTL lesions in trace conditioning, i.e. if a short delay is introduced between the CS and the UCS (Clark and Squire, 1998).

In all forms of nondeclarative memory that were mentioned so far, subjects typically acquire a new ability over repeated trials in one or more sessions. The only form of nondeclarative memory that refers to a change in performance that can be observed already after one presentation is repetition priming. The phenomenon of repetition priming is probably the most extensively studied form of nondeclarative memory.

Priming

This well known phenomenon refers to a facilitated processing of information if the same information is processed a second time (Schacter and Buckner, 1998; Schacter et al., 1993). The facilitation can be expressed in shortened reaction latencies, higher accuracy or changes in choice behaviour during the repeated processing of the information compared to the first processing of the same information. Two different forms of priming are distinguished: perceptual priming which reflects the prior processing of perceptual stimulus characteristics such as sound, form, smoothness of surface etc., and conceptual priming, which reflects the prior processing of stimulus meaning and which is, in contrast to perceptual priming, independent of the

appearance of the stimulus. Modality specific sensory neocortex is involved in perceptual priming while the left inferior frontal cortex is known to be involved in conceptual priming. Interestingly, fMRI and PET studies have revealed that priming is accompanied by a decrease of blood flow instead of an increase, a phenomenon which is also referred to as repetition suppression (Henson, 2003; Henson and Rugg, 2003; Schacter and Buckner, 1998).

As this brief overview has shown, functionally quite distinct forms of learning and memory are classified as nondeclarative memory. The functional diversity of the different forms of nondeclarative memory is also mirrored on the neural level. The different subtypes of nondeclarative memory do not share one common neural network or one neural structure, but depend on distinct, though overlapping neural networks depending on the computational demands of the tasks. Taking into account the heterogeneity of these distinct forms of learning and memory it is easier to understand that Squire and Zola-Morgan (1988) did classify them as one type of memory based on the shared absence instead of the shared presence of common features on the functional and neural level. On the functional level the different subtypes of nondeclarative memory were unified by the assumption that they are not dependent on conscious awareness for the learning episode or even the learning material. In much the same way, the neural networks underlying nondeclarative forms of memory were defined by the observation that they do not depend upon MTL structures.

> *"… it is clear that declarative memory ability can be tied to the function of the structures damaged in amnesia and that the spared (nondeclarative) memory abilities do not depend on these structures." (Squire and Zola-Morgan, 1988; p. 172)*

In short, Squire and Zola-Morgan distinguish between declarative and nondeclarative forms of memory based on the following questions:

- Does the performance depend on MTL structures or not?
- Does the performance depend on conscious awareness for the encoding episode or the learning material at retrieval or not?

Memory is classified as declarative if both questions are answered with yes and as nondeclarative if both questions are answered with no. Studies with amnesic patients and lesioned animals have provided strong evidence for the hypothesis that

declarative memory does depend upon intact MTL structures. However, whether there are forms of memory that depend on the intact functioning of MTL structures, but not on conscious awareness for the learning episode is still a matter of debate. The experiments that will be presented in this thesis addressed this question and provide data suggesting that there are indeed forms of memory depending on MTL structures but not on conscious awareness for the learning episode or the stimuli.

3.2.3 Critical remarks concerning the declarative/nondeclarative account

These apparently simple and clear distinguishing features derived from observations in severely amnesic patients bare some difficulties concerning the distinction between declarative and nondeclarative forms of memory in healthy participants. As MTL structures are non-functional in severely amnesic patients it can be excluded that performance in nondeclarative tasks is influenced by some form of declarative memory. Though, the question of whether declarative forms of memory contribute to performance in nominally nondeclarative tasks in normal participants is far more difficult to answer.

> *"…,it is often difficult to know when declarative memory, i.e. explicit attempts to recall or recognize previously presented material, makes a substantial contribution to skilled performance."* (Squire, 1992, p. 210)

There are several authors reporting that healthy participants show better performance for certain aspects of skill learning tasks, or that they acquire additional knowledge in skill learning tasks compared to amnesic patients, allowing a more flexible usage of the newly acquired skills or habits. Such observations illustrate how difficult it is, to completely rule out or to estimate the contributions of declarative forms of memory to performance in nondeclarative memory tasks in normal participants.

3.3 The distinction between explicit and implicit memory

3.3.1 Definition

The distinction between implicit and explicit memory was introduced by Graf & Schacter (1985) as follows:

> *"Implicit memory is revealed when performance on a task is facilitated in the absence of conscious recollection; explicit memory is revealed when performance on a task requires conscious recollection of previous experiences." (Graf and Schacter, 1985; p. 501).*

In explicit memory tasks, such as free recall, cued recall or recognition tasks, reference is made to the episode where the items were learned. In contrast, in implicit memory tasks no reference is made to the learning episode or even the learning material. Explicit memory refers to an intentional aspect of a retrieval process and/or to the experience of conscious recollection, including the subjective awareness that one is remembering information acquired in the past, also referred to as autonoetic consciousness by Tulving (1985). Implicit memory, by contrast, refers to unintentional retrieval processes in which previous experiences facilitate performance on tests that do not require intentional or conscious remembering of the learning episode or even the learning material. The subjective awareness that one is remembering information acquired in the past is not required. Whereas explicit memory generally can be expressed verbally, implicit memory generally can not be articulated. Schacter (1992) states that the terms explicit and implicit are quite similar to the terms conscious and unconscious and could be used interchangeably. He has chosen the more neutral term implicit, because the classical notion of "unconscious" is so closely linked to Freudian and other psychodynamic concepts, which have little in common with his concept of "implicit" knowledge.

Initially, the terms implicit and explicit were not intended to refer to hypothetical anatomically distinct memory systems such as the terms declarative and nondeclarative (Squire, 1992b; Squire, 1992a; Squire et al., 1993; Squire and Zola, 1996). However, in experimental settings, declarative memory is generally investigated with explicit memory tasks whereas the different forms of nondeclarative memory are measured by implicit tasks, indicating a close relationship between the terms declarative and explicit, or nondeclarative and implicit respectively. Currently,

the terms explicit and implicit memory are often used interchangeably with declarative and nondeclarative memory. Indirectly, this implies that the terms explicit and implicit memory as well refer to the anatomically distinct neural networks that are proposed to underlie declarative and nondeclarative forms of memory. However, recent findings suggesting an involvement of MTL structures in certain implicit memory tasks challenge this practice. Several researchers have observed an impaired performance in patients with MTL lesions in implicit memory tasks (Chun and Phelps, 1999; Curran, 1997; Rajaram and Coslett, 2000a, 2000b). Recently, other research groups have reported significant peaks of activation in MTL regions of healthy participants that performed an implicit memory task (Henke et al., 2003a, 2003b; Rose et al., 2002; Schendan et al., 2003). Elaborated experimental control makes the possibility that the MTL activations were induced by explicit memory contamination very unlikely.

Therefore I will use implicit and explicit memory as defined initially by Graf and Schacter (1985) in the following, i.e. as terms distinguishing between learning tasks that are performed with or without conscious awareness for the learning episode.

3.3.2 Critical remarks concerning the explicit/implicit distinction

While it is easy to differentiate between explicit and implicit task instructions it has turned out to be quite difficult to dissociate between the memory processes that are involved when performing a task with an explicit or implicit instruction, respectively. There are many examples where performance in an implicit memory task is influenced by explicit memory processes. The contamination of implicit memory tasks with explicit memory processes was probably most extensively studied in repetition priming paradigms (for a review see Schacter and Buckner, 1998). In a classical priming experiment, participants are shown a list of familiar words and are later given an apparently unrelated test. In a word-stem completion test for example, participants would be given a list with three-letter word beginnings and asked to complete them with the first word that comes into mind. Half of the stems could be completed with words from the previously studied list, the other half not. Priming is observed when participants provide the target completion more frequently to stems that represent studied words than to stems representing nonstudied words. Hamann and Squire (1997) have observed intact repetition priming in a severely amnesic patient despite

his recognition performance for the studied words was at chance. This indicates that word-stem completion, or similar repetition priming tests do not require explicit memory for the study list.

However, based on the observation that amnesic patients perform normal in an implicit task, the possibility that healthy participants use some form of explicit retrieval to perform in the same implicit task can not be ruled out. Indeed, a signal increase in the hippocampus during a word-stem completion task has been observed for example in a study with normal participants of Squire and colleagues (1992c). As hippocampal activation is related to retrieval success, and as priming seems to be independent from the hippocampus, the most parsimonious explanation for the reported hippocampal activation in a repetition priming task is an involuntary recollection of the studied words. This example illustrates how difficult it is to exclude that performance in an implicit task is influenced by some form of explicit memory in healthy participants, or to estimate the contributions of explicit memory contamination in explicit memory tasks. A variety of experimental strategies and criteria have been proposed to try to rule out or to estimate the contributions of explicit memory contamination (summarised in Toth, 2000). One strategy is to simply ask the participants whether they were aware of retrieving prior events while performing an implicit task, such as retrieving words from the previously studied list while performing a word-stem completion task. One well known problem with this strategy is that self-reports depend on the accuracy of the participants' memory for prior states of awareness. Furthermore, the test instructions for implicit memory tasks generally tell the participants not to intentionally retrieve prior study events. Therefore, participants who nevertheless had retrieved words from the study list, would have to admit that they ignored the test instructions. Probably not all participants would do this easily (Toth, 2000). A further possibility is decreasing the likelihood of explicit memory retrieval by using long study and test lists with a high ratio of new to old items and so decreasing as well the explicit memory contamination of implicit memory tasks. Another strategy is the process-dissociation procedure designed by Jacoby (1991) with the aim to quantify the contributions of explicit and implicit forms of memory. The process-dissociation procedure combines results from an exclusion condition, in which participants are instructed to complete word stems with words that were *not* studied, with the results from an inclusion condition, in which participants are told to complete word stems with the studied words. If a word from

the studied list is used in the exclusion (or opposition) condition, this is strong evidence that retrieval was induced by implicit memory processes, because the word would have been excluded as response, according to the test instruction, if it had been retrieved explicitly. The combination of the results of both conditions gives the possibility to estimate the contributions of the two forms of memory, i.e. implicit and explicit memory.

Explicit memory contamination is not the only difficulty that comparisons between implicit and explicit memory encompass. It is known for example that different retrieval cues can induce dissociations even in different explicit memory tasks. Words that are frequently used in language (high-frequency words) are more likely to be retrieved in free recall tests compared to seldomly used (low-frequency) words. In contrast, low-frequency words are more likely recognised than high-frequency words (summarised in Toth, 2000). Therefore, dissociations between explicit and implicit tasks are not clearly attributable to differences in the level of awareness, if different retrieval cues are used. In fact, the dissociations could have been induced by different retrieval properties of the cues rather than by the differences in the awareness level. This problem is addressed in a method, known as the retrieval intentionality criterion, which recommends providing identical cues for the implicit and explicit test and varying only the level of awareness by giving different instructions for implicit and explicit tests (Schacter et al., 1989).

Whereas the explicit memory contamination of implicit memory tasks is a generally discussed problem, the question of whether there are contributions of implicit forms of memory to explicit memory has widely been neglected so far.

3.4 Processing accounts

In a seminal paper, Craik and Lockhart (1972) offered an alternative to the declarative/nondeclarative and the implicit/explicit memory systems account, the levels of processing (LOP) account. They suggested that memory-encoding operations should be conceptualised as the processes underlying perception and comprehension and that retrieval is the logical consequence of encoding. As retrieval was assumed to reflect a re-experiencing of the initial encoding processes, no structural memory stores were assumed to exist. Memory traces were suggested to

reflect a record of the processing operations that were carried out when an event was initially experienced, i.e. the processing operations that had been necessary to perceive and to comprehend the event. They also suggested that "remembering reflected the qualitative types of analysis that had been performed during initial encoding processes of perception and comprehension, and that deeper processing was associated with higher levels of subsequent remembering" (Craik, 2002; p. 306). A series of experiments reported by Craik and Tulving (1975) provided support for these ideas. They have presented words, and each word has been preceded by an orienting question. The orienting questions intended to induce either a high level of processing, such as "Is the word a type of flower?", or a lower level of processing, such as "Does the word rhyme with train?". As they had suggested, retrieval performance was higher for words that were preceded by orienting questions inducing a higher level of processing. The level of processing controlled retrieval performance. Giving instructions that induce semantic processing is now a commonly used strategy to induce similarly deep encoding in all participants in explicit memory tasks.

However, Morris and colleagues (1977) demonstrated that rhyme-related encoding leads to higher retrieval performance than deep semantic encoding, if the retrieval test requires rhyme-recognition. They concluded that the retrieval task determines which encoding task will induce the best retrieval performance, i.e. retrieval performance depends on the specific match of the encoding and the retrieval task. Deep semantic processing is often very effective because the usual processes of recall and recognition strongly depend on semantic processing. The notion of encoding specificity is also one of the basic assumptions of the transfer-appropriate processing (TAP) framework that was developed by Roediger and colleagues (1989b, 2002). They made four assumptions. The first assumption was that retrieval tests benefit from encoding to the extent that the processes required during retrieval test overlap with the operations that were required for encoding. The second assumption was that most explicit and implicit tasks rely on different types of processing. The third assumption was that successful performance in most standard explicit memory tests, such as free recall, cued recall and recognition, depends on semantic or meaningful processing. The fourth assumption was that most standard implicit memory tests rely on perceptual information or are data-driven. Performance in these implicit memory tasks depends therefore rather on the match in perceptual

processes between study and test, than on the match in semantic or meaning-based processing between study and test.

Craik (2002) claimed that the concepts of LOP and TAP always seemed rather complementary than antagonistic to him. While rhyme specific encoding led to better recall performance in a rhyme-recognition task than semantic encoding, memory performance was substantially higher in the combination of semantic encoding and semantic retrieval than in the combination of rhyme encoding and rhyme recognition in the study of Morris and colleagues (1977). He concluded therefore that deeper encoding processes result in encoded traces that potentially are very likely to be retrieved, given that an appropriate cue is available at retrieval.

3.5 The role of medial temporal lobe structures in memory

3.5.1 The declarative/nondeclarative account

The declarative/nondeclarative account was developed to explain the pattern of impaired and spared memory performances in amnesia. Because amnesia was observed after damage of MTL structures in humans and in animals, the declarative/nondeclarative account differentiated between memory functions that are independent from MTL structures and memory functions that critically depend on MTL structures. The spared (nondeclarative) memory functions in amnesic patients (or animals) are hypothesised to be independent from MTL structures, whereas MTL structures are suggested to play a crucial role in the impaired (declarative) memory functions. It is suggested that the medial temporal lobe is required to form permanent and usable long-term declarative memory (Squire, 1992a; Squire and Zola, 1996). Long-term declarative memory is assumed to depend on the ability to establish an interaction between the neocortex and the MTL system at the time of learning. The different, relevant neocortical sites are bound together by the hippocampal system at the time of encoding. If a certain cue is processed through the hippocampus, all the sites that were activated during encoding can be reactivated by the hippocampal system, and thereby accomplish retrieval of the whole memory. From the observed temporally graded retrograde amnesia, it was concluded that memory retrieval depends only temporarily on an intact hippocampal system. Squire (1992a) hypothesised that the organization of memory storage is slowly transformed as time

passes after learning, and that the role of the hippocampal system diminishes over time until memory is independent from the hippocampal system.

3.5.2 The relational account

The relational account was developed by Cohen and Eichenbaum (1993) with the intention to define more precisely the characteristics distinguishing between declarative and nondeclarative forms of memory. The first central characteristic of declarative memory according to the relational account is that it is supported by relational representations. This means that the relevant relationships among different aspects of an event are represented in declarative memory. The relational representation of declarative memories allows first, to compare and contrast different memories and second, the inferential use of memories in novel situations. In contrast, procedural memory was suggested to involve the facilitation of particular routines for which no such processes as comparing, contrasting or making judgements about indirectly related items in novel situations can be executed. The role of the hippocampal system was suggested to be critical for the ability to form flexible relational representations.

Evidence in animals

Eichenbaum and colleagues (1996) developed a paired associates task to study the inferential use of memories in novel situations in rats. Animals were trained to associate pairs of odour stimuli with one another. For brevity, the pairs will be called A-B and X-Y where each letter corresponds to a different odour. In each trial the rat was initially presented with the first odour of one of the two pairs, i.e. A or X. Then that stimulus was removed, and a pair of odours was presented, i.e. B and Y. The rat had to learn that the choice of B was always rewarded after the initial presentation of A, whereas Y was always rewarded after the initial presentation of odour X. Animals were trained, until they reached a learning criterion of 80% correct choices in these two types of trials A-B and X-Y. Then they were trained on a second set of paired associates. The two new pairs included each one element that overlapped with the two old pairs, i.e. B-C and Y-Z. After the animals had reached the learning criterion with the new paired associates, they were trained with all four pairs, i.e. A-B, X-Y, B-C, Y-Z. Following the successful acquisition of all four pairs, the animals were tested in two critical probe tests for inferential expression. The aim of the probe tests was to

determine whether the overlapping odour pairs were represented as two sequences of three odours, (A-B-C and X-Y-Z), or whether the four odour pairs were represented independently from each other. In the transitivity test, the first of one of the two odour sequences was initially presented (i.e. A or X). Then the animals had to select between C and Z, two stimuli that were only indirectly related with the initially presented stimulus via the shared associate B or Y respectively. The correct choice of the indirectly related stimulus requires the ability to make inferential use of memories in a novel situation, i.e. the animals had to infer that A is indirectly related to C via B, without having trained this association before. If animals are able to recognize this indirect linking, they will show a preference for C compared to Z after the initial presentation of A. Whereas animals with hippocampal lesions were not impaired in learning the paired associates compared to normal rats, they were severely impaired in the transitivity task, showing no preference for the indirectly related odour. Normal rats showed a clear preference for the indirectly related odour, indicating that they are able to make judgements about new pairings based on the acquired relations between the paired associates. In the symmetry test, the animals had to recognize the odour pairs in the reverse order of that used during training, i.e. C-B or Z-Y. The correct choice required the ability to recognize the related pairings regardless of the order in which the different odours are presented. Normal animals again showed a preference for the related odour, regardless of the presentation order, whereas animals with hippocampal lesions were severely impaired. Based on these data, they concluded that the hippocampal formation is critical for the acquisition of the representation of paired associates that allow flexible and inferential judgements about the same items, when they are presented in unusual ways.

Evidence in humans

In a review paper Cohen and colleagues (1999) summarised the data from functional neuroimaging studies in combination with neuropsychological findings. They tested these data against the following five different explanatory accounts for the role of the hippocampal system (hippocampus and related MTL structures such as entorhinal, perirhinal and parahippocampal cortices):

1. Novelty detection: The role of the hippocampal system in memory includes detecting novel stimuli and encoding information about those stimuli in memory.

2. Retrieval success: The hippocampal system is involved in the successful retrieval of previously stored information.
3. Explicit (vs. implicit) memory: The hippocampal system plays a critical role in explicit memory.
4. Spatial (cognitive) mapping: The hippocampal system plays a crucial role in spatial memory, permitting the ability to construct, maintain, and make use of spatial maps.
5. Relational memory processing: The hippocampal system is critically involved in memory binding or relational memory processing, i.e. binding the converging inputs from various processors, allowing to form representations of the relationships among the constituent elements of scenes or events.

They conclude that the relational account can accommodate the full range of the imaging data and the neuropsychological findings better than any other account. The involvement of the hippocampal system in the other tested accounts can be explained with the necessity to acquire or to retrieve new relations. Therefore, the other accounts can be integrated in the relational account. For example, concerning the novelty detection account, one would expect more relational binding and encoding, when a stimulus is processed for the first time compared to when the same stimulus is processed repeatedly and therefore more activation of the hippocampal system when processing a novel scene compared to one that already had been seen.

The relational account was initially developed as a more elaborated version of the declarative/nondeclarative account. However, recent data suggest that relational learning and declarative memory can be dissociated. These newer findings indicate that the hippocampal system is involved in relational learning irrespective of whether conscious awareness for the learning episode is present or absent and were integrated in the current version of the relational memory account:

> *"The more recent elaboration of the theory into the current relational memory account, i.e. that the role of the hippocampal system is in binding together multiple streams of information, regardless of whether memory is tested explicitly or implicitly (…) permits this framework to accommodate a huge body of findings in the human and animal literatures, including both, neuropsychological and neurophysiological data."* (Cohen et al., 1999; p. 96)

With the assumption that the hippocampal system is involved whenever relational binding takes place, irrespective of the level of awareness (Cohen et al., 1999; Eichenbaum, 1999), the relational memory account is in contrast with the hypothesis of the declarative/nondeclarative account, where the hippocampal system is suggested to play a role exclusively in declarative forms of memory. Findings supporting the current relational memory account will be summarised in the next section.

3.5.3 Involvement of MTL structures in implicit memory tasks in humans

Recent data suggest that MTL structures are not exclusively involved in explicit forms of memory, but play also a role in certain forms of implicit memory. There are a few observations of impaired associative priming in amnesic patients with severe bilateral damage of the hippocampal formation suggesting a role for the hippocampal formation in certain forms of nondeclarative memory. The first study without the limitation of probable "explicit contamination" of the implicit task was presented by Chun and Phelps (1999). In their study, participants task was to detect rotated T targets among rotated L distracters on a visual display. In each session, a set of new visual contexts was generated by manipulating the spatial configurations of the items in the search display. One set of spatial contexts was presented repeatedly across blocks of trials throughout learning (old condition), to examine contextual learning. In old displays the targets appeared always at identical locations within their invariant contexts. Therefore, the visual context predicted the target locations, facilitating the search task in old compared to new displays. Normal participants were not able to discriminate between old and new displays. Therefore, the benefit of visual context information in old displays was concluded to be induced by implicit memory for the visual context. The amnesic patients in the study of Chun and Phelps (1999) did not demonstrate any beneficial effect of old compared to new visual contexts, suggesting a role for MTL structures in implicit tasks requiring the binding of multiple cues. The absence of contextual learning did not reflect a general learning impairment, as the amnesic patients showed normal implicit perceptual/skill learning independent of context information, indicated by a decrease in overall search reaction times over the session.

MTL damage in two amnesic patients in the study of Chun and Phelps (1999) was not restricted to the hippocampal formation but included some additional atrophy of the surrounding temporal lobe. Manns and Squire (2001) studied learning in patients with damage confined largely to the hippocampal formation using the same task as Chun and Phelps (1999). They reported that patients with damage restricted largely to the hippocampal formation showed beneficial effects of repeated visual contexts, whereas patients with extensive damage to MTL together with variable damage to the lateral temporal cortex did not benefit from the repeated visual contexts. Based on these findings they concluded that contextually specific perceptual learning is not dependent from the hippocampal formation and that damage limited to the hippocampal formation does not impair nonconscious memory. Indeed, if the displays can be represented as one picture, normal performance in the contextual learning task might not require the formation of flexible relations and hence rather depend on intact perirhinal cortices, than on an intact hippocampus, as the perirhinal cortex is suggested to be critically involved in recognition of single items (Aggleton and Brown, 1999; Brown and Aggleton, 2001; Davachi et al., 2003).

Similar results as reported by Chun and Phelps (1999) have been observed using verbal paired associate learning tasks. Savage and colleagues (2002) for example compared the performance of patients that had undergone left-sided anterior temporal lobectomy (LATL) with patients that had undergone right-sided anterior temporal lobectomy (RATL) for the relief of temporal lobe epilepsy. They used a masked priming paradigm to measure memory for the word pairs implicitly. Whereas Savage and colleagues observed evidence for implicit memory for the word pairs in RATL patients, no similar effect had been observed in LATL patients. In LATL the lesion was located in the hemisphere that is specialised for the memory of verbal information. In another study, Yang and colleagues did observe impaired priming for new verbal associations despite normal levels of item priming using two different tasks in patients with selective damage to MTL structures (Yang et al., 2003).

Furthermore, recent fMRI studies have directly addressed the question of whether MTL structures are engaged in certain implicit memory tasks and did indeed observe activity changes in MTL structures in healthy participants performing implicit memory tasks (Henke et al., 2003b; Henke et al., 2003a; Rose et al., 2002; Schendan et al., 2003).

Rose and colleagues (2002) for example, observed increased activity in the ventral perirhinal cortex while participants learned flexible relational contingencies without awareness. The version of the number reduction task (NRT) they used had been developed by Frensch and Haider (2003). Participants were presented with a string of eight digits on a computer screen. The strings were constructed of the three different digits "1", "4", and "9". Participants were instructed to process the strings pairwise from the left to the right following two rules. According to the first rule, the "same rule", the result of two identical digits was always the digit itself, i.e. "4 4" resulted in "4". According to the second rule, the "different rule" the result of two different digits was always the remaining third digit, i.e. "1 4" resulted in "9". So, the participants were engaged in an explicit learning task requiring that fixed stimulus-response mappings were learned. In addition to these overt rules the following abstract "hidden structure" was implemented in the NRT: The responses of the last three input positions were always the mirror image of the responses for the previous three input positions, i.e. the last three responses on input positions 5, 6, and 7 were always determined by the three responses before on input positions 2, 3, and 4. This principle was underlying all response patterns, irrespective of the concrete stimulus-response associations in a certain trial. Furthermore, this regularity was only present in the response patterns but not in the displayed strings. The authors hypothesised, that reaction times for the determined response positions, 5, 6, and 7 should become increasingly faster with the participants becoming more sensitive to the hidden rule, indicating that the hidden structure was learned implicitly, i.e. that the participants acquired relational contingencies in the absence of conscious awareness. The final result of the whole string was always identical to the second input. Therefore, participants could reduce the number of inputs if they gained explicit knowledge about the hidden structure, because they knew the final result after the second input. This possibility was outlined to the participants during the instruction as an option to speed up trial processing, whenever they knew the final result before entering all previous results. Such a strategy shift (i.e. reduced number of responses per trial) would be easily detectable and allowed Rose and colleagues (2002) to control for explicit memory. Implicit learning of the sequential regularities of the hidden rule activated the perirhinal cortex, an MTL structure. Conversely, explicit learning of fixed stimulus-response associations engaged basal ganglia and the cerebellum. The authors concluded from these data, that the functional segregation of the MTL and

the basal ganglia can depend on the type of material that is learned and not necessarily on the participants' awareness for stimulus contingencies. Moreover, their data suggests an involvement of MTL structures in the extraction of sequential relationships, even in the absence of conscious awareness for the acquired relations.

Schendan and colleagues (2003) studied the neural substrates of implicit and explicit sequence learning with fMRI. Participants performed a SRTT. They were presented with four white outline squares on a black background and four response keys with each key corresponding to one of the four squares. As soon as one of the squares lit up as filled white square, they had to press corresponding key as fast as possible. On some SRTT blocks one sequence of locations was repeated, whereas on others new sequences of random locations were presented. The repeated sequences used by Schendan and colleagues (2003) required the acquisition of higher order associations between multiple locations. The choice of this learning task had been motivated by a study of Curran and colleagues (Curran, 1997) suggesting that amnesic patients are impaired in acquiring sequences that can not be learned based on simple frequencies or contingencies between one location and a second but require the learning of higher order associations between multiple locations. Schendan and colleagues (2003) reported evidence that both implicit and explicit learning of higher order sequences involve MTL structures, specifically the hippocampal formation. They concluded from their findings that the early acquisition phase of temporal sequence learning engages the hippocampus, irrespective of whether learning is implicit or explicit. They claimed that these findings are in full agreement with the relational account suggesting that the associative and temporal structure of the representation that is being acquired determines the hippocampal engagement rather than the level of awareness.

In an fMRI experiment Henke and colleagues (2003a) reported activity changes in the hippocampal formation while participants encoded and retrieved face-profession associations in the absence of awareness. The fMRI experiment consisted of two time-series, the first measuring neural correlates associated with nonconscious encoding and the second measuring neural correlates associated with nonconscious retrieval of face-profession associations. During the first time-series (implicit encoding) face-profession pairs were presented briefly and preceded and followed by visual noise patterns to exclude conscious perception of the stimuli in the experimental condition. In the control condition a head contour with no profession

added was maskedly presented. The subjective impression of the masked presentation did not differ between the experimental condition (masked presentation of face-profession pairs) and the control condition (masked presentation of head contour) and consisted of moving grains, interrupted by a visual fixation cross for both conditions. In the second fMRI time series, designed to test for nonconscious retrieval of the faces and the face-profession associations, the faces were presented again, with no professions added and without masks for 3s each in the experimental condition. In the control condition novel faces, that had not been presented previously were shown. The task in both conditions was to guess the professional category of a profession associated with each presented face (academic, artist or workmen) and to press one of three keys accordingly. Henke and colleagues reported significant activity changes bilaterally in the hippocampus and in the right perirhinal cortex during nonconscious retrieval of the faces and the face-profession assocations. Furthermore, there was a trend toward left hippocampal activation during the nonconscious encoding of the face-profession associations. However, the design of this study (Henke et al. 2003a) did not allow the authors to distinguish between the contribution from nonconscious face retrieval and from nonconscious face-profession retrieval to MTL activation.

Therefore, Henke and colleagues (2003b) replicated their findings in a second study with a slightly changed design, allowing to differentiate between memory for faces and memory for face-word associations. For this purpose, the control condition for nonconscious encoding was adapted accordingly. Instead of head contours, faces with no professions added were maskedly presented in the control condition of nonconscious encoding of the second study. Contrasting the masked presentation of face-profession pairs with the masked presentation of faces alone was hypothesised to isolate the cognitive processes underlying reading and understanding the professional and associating the meaning of the word with the face. Based on the results presented in their second study (Henke et al. 2003b) the authors concluded that the reactivation of semantic (face-word) associations alone is sufficient to increase MTL activity. Moreover, significant activity changes in the hippocampus and the perirhinal cortex had been observed during nonconscious encoding.

The data of these two studies (Henke et al. 2003a, 2003b) are evidence suggesting a role of the hippocampal in the formation and the retrieval of new semantic

associations, and support the hypothesis that the hippocampus is involved in the formation of new associations irrespective of the level of awareness.

To summarize, all studies providing evidence suggesting a role of MTL structures also in implicit forms of memory have in common that the used tasks required that the participants linked different, previously unrelated pieces of information during encoding (Henke et al. 2003a, 2003b; Rose et al. 2002; Schendan et al. 2003). Thus, these findings provide increasing evidence for the hypothesis that the hippocampal formation is involved in the formation of flexible relations, irrespective of the level of awareness, and against models for long-term memory that propose an exclusive role of the hippocampal formation in explicit or declarative memory tasks.

4 The present study

4.1 Hypotheses

Until recently, it has been widely accepted that implicit memory tasks are independent from MTL structures. Moreover, if involvement of MTL structures in implicit memory tasks was observed, this could generally be explained as effect of explicit memory contamination. However, this view has been challenged by several recent studies that have directly addressed the question of whether MTL structures play a role in implicit forms of memory. The data they have reported support the hypothesis that MTL structures are also involved in implicit memory tasks, if the processing demands of the implicit task involve the formation of new associations between previously unrelated items. Thus, the debate of whether MTL structures indeed play a role in implicit memory tasks is opened.

However, two further aspects in the discussion about the distinction between different forms of long-term memory have been widely neglected so far. First, the question of whether implicit learning has an influence on explicit learning. Second, the question of whether implicitly formed new associations share any of the criteria associated with explicit or declarative memory, such as flexibility or compositionality (assuming that it is possible to establish new associations in the absence of conscious awareness). The present doctoral thesis presents an attempt to address these two questions.

To our knowledge, there is only one fMRI study by Wagner and colleagues (2000) that directly investigated the influence of priming, a nondeclarative form of memory, on performance in episodic learning, a declarative form of memory. They found experimental evidence for their hypothesis that priming can inhibit episodic encoding. In their study, subjects encoded a list of words containing three types of word trials: re-encoding of words they had already studied the day before, re-encoding of words they had studied immediately before, and encoding of new words. For the words that were re-encoded after a delay of 24 hours, Wagner et al. (2000) predicted a smaller priming effect than for the words that were re-encoded after a short delay, since most priming effects are transient and get smaller with increasing delay time. They hypothesised that larger priming effects produce worse declarative learning, because

large priming reduces neural activity in brain areas, which are also engaged during declarative learning and which should be strongly active, if declarative learning were to be effective. In their fMRI data this effect could be observed in a smaller increase in blood flow during the re-processing of a stimulus, compared to the first processing of the stimulus. This phenomenon is now also referred to as repetition suppression (Henson, 2003; Kiefer et al., 2000). As predicted, they could observe larger priming effects for the short than the long lag (shorter reaction times and stronger reduction of neural activation) as well as worse delayed recall of words that were re-encoded after a short than a long lag. They suggest that priming may impair new declarative learning and subsequent recall by reducing encoding variability. This interpretation is based on evidence that encoding variability enhances the recall from declarative memory, because the encoding of multiple event attributes provides multiple retrieval routes to a particular episodic memory.

The study of Wagner and colleagues (2000) provides evidence that priming has an impairing effect on subsequent episodic learning. This effect was also assumed to underlie the spacing effect that is usually observed in explicit memory tasks in a purely behavioural study (Mammarella et al., 2002). The spacing effect refers to the phenomenon that repeated items within a list, are usually better remembered if the repeated presentations are separated by the presentation of several intervening items (spaced items), compared to items where the repeated presentations are not separated by the presentation of intervening items (massed presentation).

Based on the observation that a large priming effect is coupled with weak performance in an explicit retrieval task, whereas a small priming effect is coupled with better performance in an explicit retrieval task, it can be hypothesised that the two different neural networks underlying priming and explicit memory retrieval interact competitively. A similar observation of competitive interactions between declarative and nondeclarative forms of memory has also been made using a probabilistic classification learning task, depending on whether the task instruction emphasised nondeclarative (learning based on trial-by trial-feedback) or declarative memory (learning of paired associates; Poldrack et al., 2001). Thus, one might speculate that nondeclarative forms of memory have impairing effects on declarative memory and vice versa, because the different involved neural networks interact competitively.

However, it could easily be imagined that beneficial effects of implicit learning on later explicit learning and retrieval would be observed, if the used implicit task involves the same neural network as the explicit learning task. In terms of the TAP account, this would require that the processing demands of the implicit and the explicit task are matched. According to the declarative/nondeclarative account however, MTL structures are crucial for performance in explicit memory tasks, whereas performance in implicit memory tasks is independent from MTL structures. Hence, developing an explicit and an implicit task depending on the same neural network would be an impossible mission. Though, as already mentioned, increasing evidence suggests that MTL structures play a role in implicit learning tasks, if they involve associative learning and retrieval, i.e. if the tasks require processing demands that are typically involved in explicit learning and retrieval tasks. Henke and colleagues (2003a) have observed a similar network - including the hippocampal formation – engaged, while participants where learning and retrieving face-profession associations, irrespective of whether participants were doing the task with or without conscious awareness. The involvement of the hippocampal formation in implicit encoding of face-profession associations had been replicated in a slightly changed paradigm, allowing to dissociate between memory for face-profession associations and memory for faces alone (2003b) and therefore providing evidence, that the signal changes in the hippocampus had indeed been induced by implicitly associating the faces and the professional words.

Based on the evidence indicating that the hippocampus is relevant for both, implicit and explicit associative learning, we expected an interaction between implicit and explicit associative learning. However, given that the same neural structures are crucially involved in both, implicit and explicit associative learning, we expected not a purely competitive interaction as had been observed when comparing implicit and explicit tasks depending on different neural networks and requiring different processing demands (Poldrack et al., 2001; Wagner et al., 2000). We therefore hypothesised that the effects of implicit on explicit learning would be facilitatory or inhibitory, depending on whether the implicitly learned information is semantically congruent or incongruent to the explicitly learned information. Furthermore, we hypothesised that the modifying effect of implicit on explicit learning would be mediated by the hippocampus.

The second point addressed in this doctoral thesis concerns the quality of implicitly formed associations. It is still fairly widely held that implicit memories are rigid and lack the flexibility of explicit memories. The ability to form flexible new relations is assumed to depend critically on the hippocampal formation. Therefore, the increasing evidence indicating a role of the hippocampal formation also in implicit memory tasks challenges the view about the quality of implicitly formed associations. If the role of the hippocampal formation is indeed to establish flexible relations between previously unrelated parts of an event, and if the hippocampus is indeed involved in the implicit formation of new relations, one could easily imagine, that the flexibility of memories depends rather on the question of whether the task depends on the functioning of the hippocampus than on the question of whether the relations had been formed in the absence or presence of conscious awareness. The question of whether the formation of flexible relations is dependent on the involvement of conscious awareness for the relations has been addressed by Greene and colleagues (2001). Their results suggest that relational learning tasks do not necessarily require conscious processes. Hence, implicitly formed memories might also rely on flexible representations. In their experiment, participants were assigned to one of two groups, either informed or uninformed. Participants assigned to the informed condition were told that the task involved making transitive inferences from premise pairs. Participants of the uninformed group were simply told that they had to learn the premise pairs by trial and error. During the training phase, participants were presented with pairs of characters. They had to choose one of the two characters, whereas one character was always correct and the other was always wrong. So, the participants learned, which of the two characters of each pair of a set of four overlapping premise pairs was correct (A>B, B>C, C>D, D>E; ">" indicates the correct choice is on the left). These overlapping premise pairs could either be encoded as four distinct pairs, or as hierarchically ordered sequence (A>B>C>D>E). During the training phase, participants got always feedback indicating whether their choice had been correct or not. In the test phase, pairs of characters were presented again, and participants had to select one character in each trial. However, no feedback was given during the test phase. The presented pairs during test included all four premise pairs of the training phase. To test whether the overlapping premise pairs had been encoded hierarchically rather than as four distinct pairs, the transitive pair B>D had been included to assess the capacity for transitive inference. Participants of the uninformed

group were given a postexperimental awareness assessment. Both, participants of the informed and the uniformed condition learned the premise pairs at better than chance levels. More importantly, both, the informed and the uninformed participants showed above chance performance in the critical BD probe test for the capacity of transitive inference. Moreover, performance on the transitive task did not correlate with test awareness in the group of the uninformed participants. This is evidence, suggesting that awareness of a transitive relationship is not a necessary prerequisite for the capacity of transitive inference. However, potential differences between uninformed and informed participants could have been masked by a ceiling effect in this first experiment. Therefore, Greene and colleagues (2001) carried out an additional experiment with a slightly changed design and a new group of participants. All participants were assigned to the uninformed group. This time, they tested for transitive inference at the end of each training block, and interrupted training as soon as performance in the B>D test reached the end level observed in the previous experiment (i.e. 7 correct choices out of 8). Participants were then given the post-experimental awareness assessment. If the training was interrupted as soon as B>D performance reached the end level, post training awareness was decreased across participants. This suggests that awareness of a transitive relationship does not increase before performance in the B>D test reaches the end level. Indeed, additional training after the performance level has reached the end level increased the level of awareness. The authors concluded from these results that there is not a necessary relationship between awareness of a transitive relationship and transitive performance. Hence, their results provide additional support for the hypothesis that implicit tasks may rely on flexible representations (Willingham, 1997).

In our study, participants implicitly learned face-profession associations previous to the explicit learning of an association between the same face and a different profession. We assumed that implicitly learned face-profession associations modify subsequent explicit learning only if the face and the profession had been encoded as two related but separate semantic entities. At the time of explicit encoding of the face-profession association the participant has to recognize that *this* face had previously been presented in relation with a *different*, semantically incongruent or congruent profession. Therefore, the observed modifying effect of implicitly formed semantic associations on explicit learning and retrieval of semantic associations

provides additional support for the hypothesis that implicit tasks rely on flexible representations.

To summarize, the following hypotheses had been addressed in the present study (chapter 5):

1. New semantic associations can be established implicitly, i.e. in the absence of awareness for the stimuli and the learning episode.
2. Implicitly formed semantic associations modify subsequent explicit learning and retrieval. The influence of implicit on explicit associative learning will be inhibiting or facilitating, depending on whether the semantic content of implicit and explicit associations is conflicting or congruent:
   2a. Implicit learning of semantic associations *impacts* subsequent explicit learning and later recall of *incongruent* semantic associations.
   2b. Implicit learning of semantic associations *improves* subsequent explicit learning and later recall of *congruent* semantic associations.
3. The neural network mediating the potential modifying effect of implicit learning of semantic associations on subsequent explicit learning of semantic associations involves MTL structures.

In addition, the finding of a modifying effect of implicitly formed semantic associations on subsequent explicit encoding and retrieval would question the view, that implicitly formed semantic associations consist of rigid, fused or noncompositional representations.

4.2 Methods: Comments on behavioural approach

4.2.1 How to avoid explicit memory contamination

The aim of our study was to demonstrate that implicit learning has a modifying effect on later explicit learning and retrieval. Because we were not interested in interactions between different forms of explicit memory it was of crucial importance to avoid that performance in the implicit task could be contaminated by some form of explicit learning. It seems reasonable to assume that the absence of conscious perception of the learning material is a very effective method to exclude confounding effects of explicit learning on implicit learning. Thus, we decided to present the stimuli for

implicit learning of face-profession associations below the objective awareness threshold for the presented stimuli, i.e. subliminally.

However, conscious perception of a stimulus is rather a continuous than a clear-cut process. Cheesman and Merikle (1984) addressed this problem with a pragmatic approach. They proposed a distinction between subjective and objective measures of conscious perception (Figure 6). Subjective measures typically rely on a personal verbal statement, indicating that he or she did not detect the presence of a target stimulus. If a participant states that he or she did not detect the presence of a target stimulus it can be concluded that the stimulus had been presented below the subjective awareness threshold according to Cheesman and Merikles (1984). Objective measures by contrast, typically involve two-alternative forced choice-tasks in which participants have to choose between the presented target and a non-presented distracter stimulus, although they feel that they are just guessing. If their performance is at chance, i.e. the target stimulus is selected as often as the distracter, it can be concluded that the stimulus had been presented below the objective awareness threshold according to Cheesman and Merikle (1984).

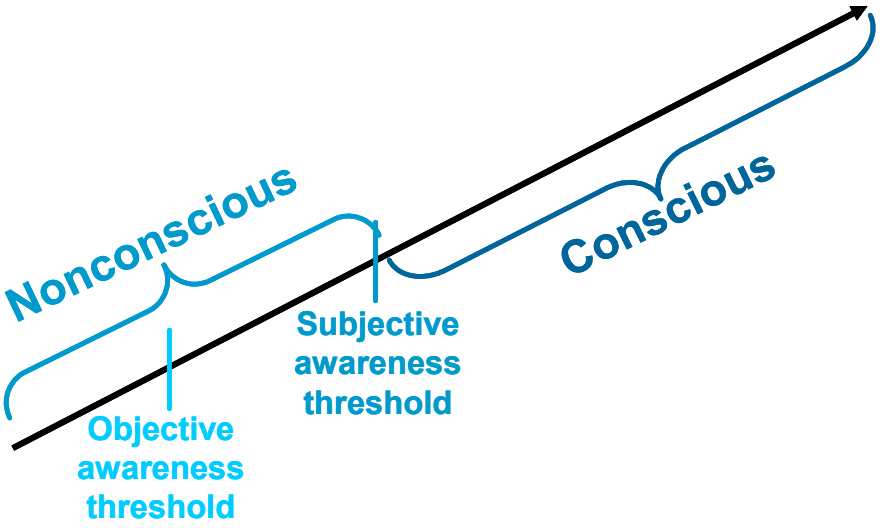

Figure 6. Conscious awareness for a stimulus increases continuously. Cheesman and Merikle (1984) proposed a distinction between two different levels of nonconsciousness based on objective and subjective measures of awareness.

We decided to present the stimuli below the objectively defined awareness threshold to minimize the risk that the presented stimuli reach conscious awareness and so the risk that implicit learning is contaminated by some form of explicit learning. For this purpose, we used a visual backward masking paradigm (Henke et al., 2003b, Figure 7). Masking methods render stimuli invisible to the conscious mind by interrupting neural responses to masked stimuli (Rolls & Tovee, 1994; Kovacs et al., 1995).

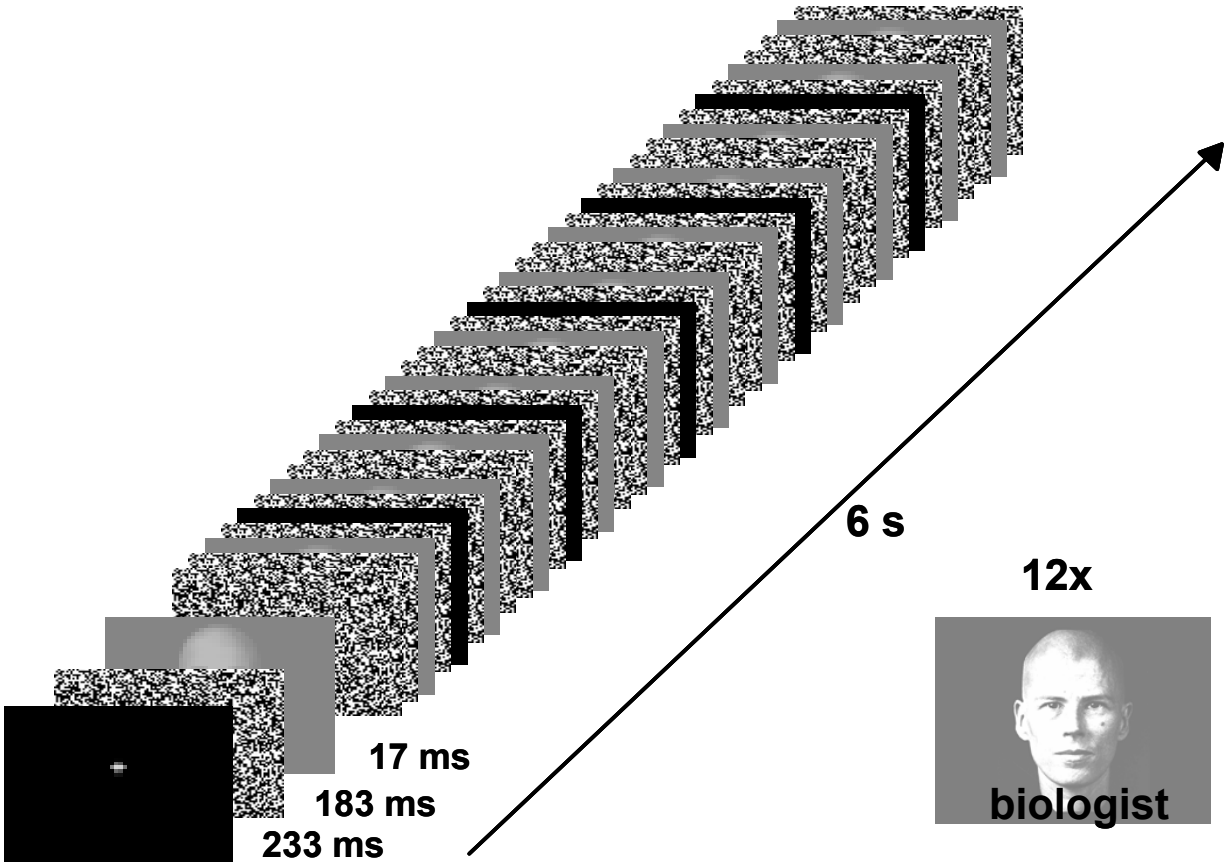

Figure 7. Masking method adapted from Henke et al. (2003b). A stimulus (S) was presented 12 times within 6s for 17 ms. Visual noise masks (M) were presented for 183 ms and a fixation cross (F) or a vertical or a horizontal bar was presented for 233 ms. The stimulation sequence for one trial was F - M - S - M - M - S - M - F - M - S - M - M - S - M - F - M - S - M - M - S – M - F - M - S - M - M - S - M - F - M - S - M - M - S - M - F - M - S - M - M - S – M. The subjective perception of this presentation consisted of moving grains interrupted by visual fixation slides.

4.2.2 How to approach the questions - basic idea

We used an adapted version of our implicit face-profession association paradigm (Henke et al., 2003a, 2003b). Explicit learning of face-profession associations was always preceded by implicit learning of the same faces combined with different professions. The first experiment was designed to test for inhibitory effects of implicit learning on subsequent explicit learning and retrieval. The second experiment was designed to test for facilitating effects of implicit learning on later explicit learning and retrieval. To test for inhibitory effects we induced semantic incongruence between face-profession associations that were to be learned implicitly and explicitly. Face-profession pairs were flashed briefly and preceded and followed by visual pattern masks for implicit associative learning. Based on previous findings from Henke and colleagues (2003b), we assumed that the faces and the professions would be linked implicitly during the masked (subliminal) presentation, although participants were not aware of the presented face-profession pairs. For the subsequent explicit associative learning the same faces were presented again (6 s, no masks) this time they were, however, combined with new, semantically conflicting professions (e.g., implicit learning: face A with magician; explicit learning: face A with jurist; Figure 8). To test for facilitating effects we used semantically congruent face-profession pairs for implicit and explicit learning. As in the first experiment, face-profession pairs were flashed briefly and preceded and followed by visual pattern masks for implicit associative learning. For the subsequent explicit associative learning the same faces were presented again but this time combined with new, yet semantically congruent professions (e.g., implicit learning: face A with lawyer; explicit learning: face A with jurist; Figure 8). Notice, that we did not use identical professional words for implicit and explicit learning to induce the facilitating effect. Using a professional word that is semantically closely related but is perceptually different during implicit learning has the advantage, that we can exclude visual priming effects induced by the identical professional word. The results of a pilot study we conducted previously to our imaging experiments have shown, that visual priming effects indeed might contribute substantially to effects of the masked presentation of face-professions on subsequent explicit learning of identical face-profession associations (Pröll, 2002). An additional fMRI experiment, in which identical stimuli were presented for implicit and explicit learning, was included later on advise of an external reviewer (for details see manuscript).

All experiments included a neutral condition in which twelve masked faces were combined with nonwords (e.g. bdfper) instead of written professions to leave subsequent explicit learning uninfluenced by implicitly formed semantic face-profession associations. Face priming and non-semantic forms of associative priming were present in both conditions in each experiment. The instruction for explicit learning was to imagine the presented person in a typical scene of the indicated profession. This task automatically induces the semantic binding of the profession to the face.

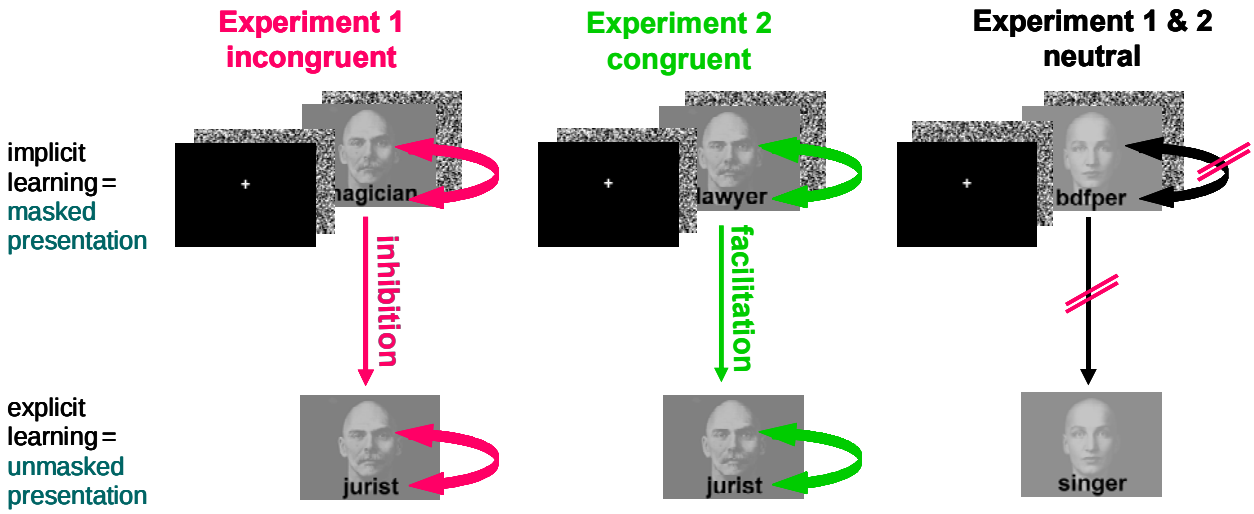

Figure 8. The masked presentation of a face-profession pair was hypothesised to *inhibit* subsequent learning of a *semantically incongruent* face-profession pair (Experiment 1). Conversely, the masked presentation of a face-profession pair was hypothesised to *facilitate* subsequent learning of a *semantically congruent* face-profession pair (Experiment 2). In the neutral condition masked face-nonword pairs had been presented. Because the nonwords do not contain any meaning, the faces can not be linked to any semantics during the masked presentation. Therefore, subsequent learning of face-profession pairs is hypothesised to be uninfluenced by any implicitly learned semantic associations in the neutral condition (Experiment 1 and 2).

The masked presentation of four face-profession pairs was always followed by the supraliminal presentation of the corresponding face-profession pairs (same faces combined with new, semantically congruent or incongruent professions) in the same order. Using this “block design” we achieved a constant interval of 18s between implicit and explicit learning of the face profession pairs. (e.g., implicit learning: face

A with magician; explicit learning: face A with jurist; Figure 9). Furthermore, a modifying effect of implicit on explicit learning and retrieval will only be observed with this design if each subliminally presented face had been linked to its profession (Figure 9).

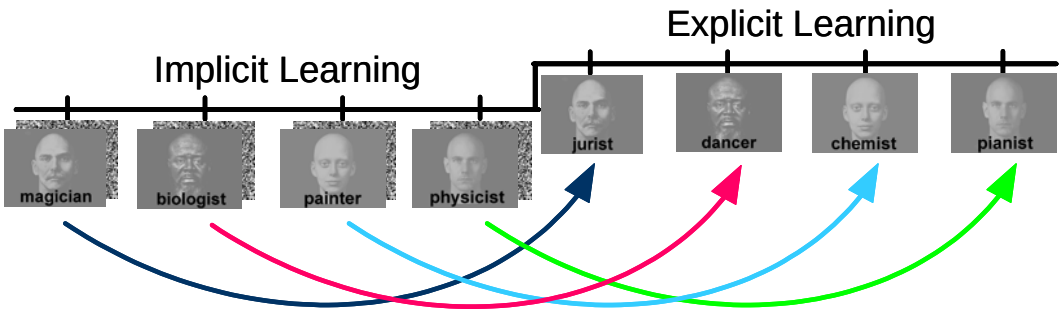

Figure 9. Because the corresponding face-profession pairs are not presented for explicit learning immediately after the masked presentation, we hypothesize, that implicit learning will only modify explicit learning if the faces and the professional words had been linked during the masked presentation (implicit learning).

A fourth, purely behavioural control experiment was conducted with a further group of participants to test for implicit effects of the masked professions alone on explicit face-profession learning. For this purpose, the professional words were presented in combination with a head contour (always the same head contour) for implicit learning (see Figure 10). Explicit learning of the face-profession pairs was identical to the two other experiments (see Figure 8). We also included a neutral condition in which the head-contour was combined with nonwords.

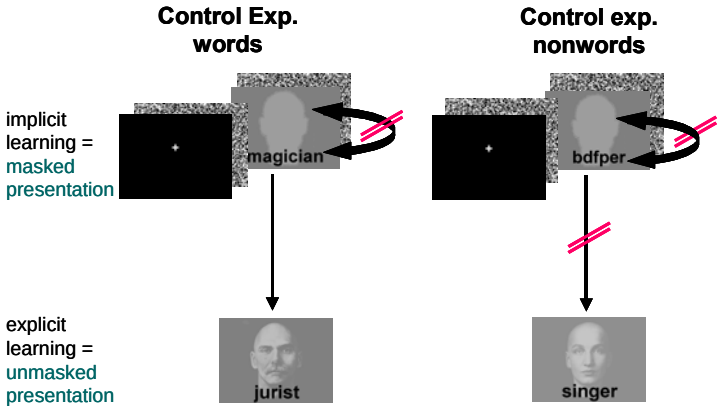

Figure 10. In the control experiment the professional words had been combined with a head contour (the same head contour for all stimuli) and not with faces during the masked presentation. Because the professional words can not be linked semantically to a specific

face, any effect of the subliminally presented stimuli can be put down to an effect of the subliminal presentation of professional words alone.

Because the professional words can not be linked semantically to a specific face, any modifying effect of the masked presentation of the contour-profession pairs on subsequent explicit learning can be put down to an effect of the masked presentation of the professional word alone.

To test for differences in the explicit retrieval performance the same task was used in all three experiments. Minutes after learning all faces were presented again as retrieval cues with the instruction to remember the (explicitly) associated professions and to indicate which professional category - academic or artist - the retrieved professions belong to. This semantic translation ensured that semantic rather than non-semantic face-profession associations were being retrieved.

4.2.3 General experimental design

The general design was identical in all three experiments. In this section, a brief overview over the common “time line” (Figure 11) and the commonalities in the experimental design of the three experiments will be given. A more detailed description of the experimental design of the different experiments is included in chapter 5 (Manuscript).

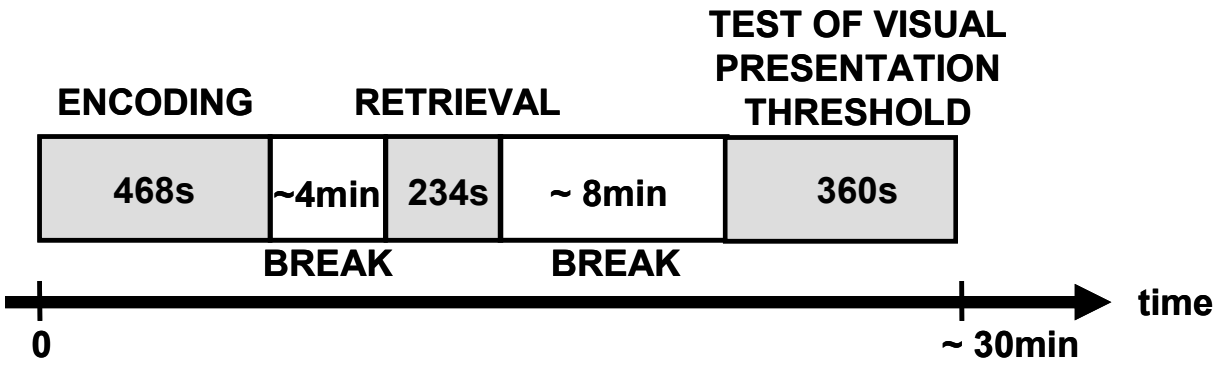

Figure 11. The presented “time line” was identical in all experiments.

In each experiment, participants started with the time-series for encoding after they had been instructed and placed in the MR-scanner. About four minutes after the time-

series for encoding, the time-series for retrieval took place. Following the retrieval task, participants underwent a step by step debriefing while still lying in the MR scanner. After debriefing, the visual presentation threshold was tested in a further run to ascertain that the subliminal stimuli had been presented below the objective awareness threshold (see Figure 11). During the time series for encoding and retrieval fMRI data was collected. No fMRI data was measured during the visual presentation threshold.

The same block design was used for the encoding and the retrieval time series in all four experiments. The duration of each block was 24s. During one block always four stimuli were presented within 6s. The general block design of the encoding and the retrieval time series will be explained below. For details about the task instructions and the stimuli used in the control experiment see chapter 5.

Each encoding time series consisted of blocks of six different conditions (see Figure 12). The six conditions were a masked baseline condition (Figure 12, A; identical in all experiments), implicit encoding of the experimental condition (Figure 12, B; different stimuli used for the different experiments), explicit encoding of the experimental condition (Figure 12, C; identical stimuli used for the different experiments), unmasked baseline (Figure 12, D, identical in all experiments), implicit encoding of the neutral condition (Figure 12, E; identical in all experiments), explicit encoding of the neutral condition (Figure 12, F; identical in all experiments).

A block of four supraliminal face-profession pairs (C or F) was always preceded by a block of masked presentations of the same four faces (B or E). For the implicit encoding in the experimental condition (B) these masked faces were either combined with new professions that were semantically incongruent to the supraliminal professions (Experiment 1, incongruent; shown in Figure 12 lower panel), semantically congruent (Experiment 2, congruent) or with the same professions (Experiment 3, identical). For implicit encoding in the neutral condition (E) the masked faces were combined with nonwords in all experiments (see Figure 12 lower panel). During all blocks in which the stimuli were presented with masks, the same masking method was used (Figure 7).

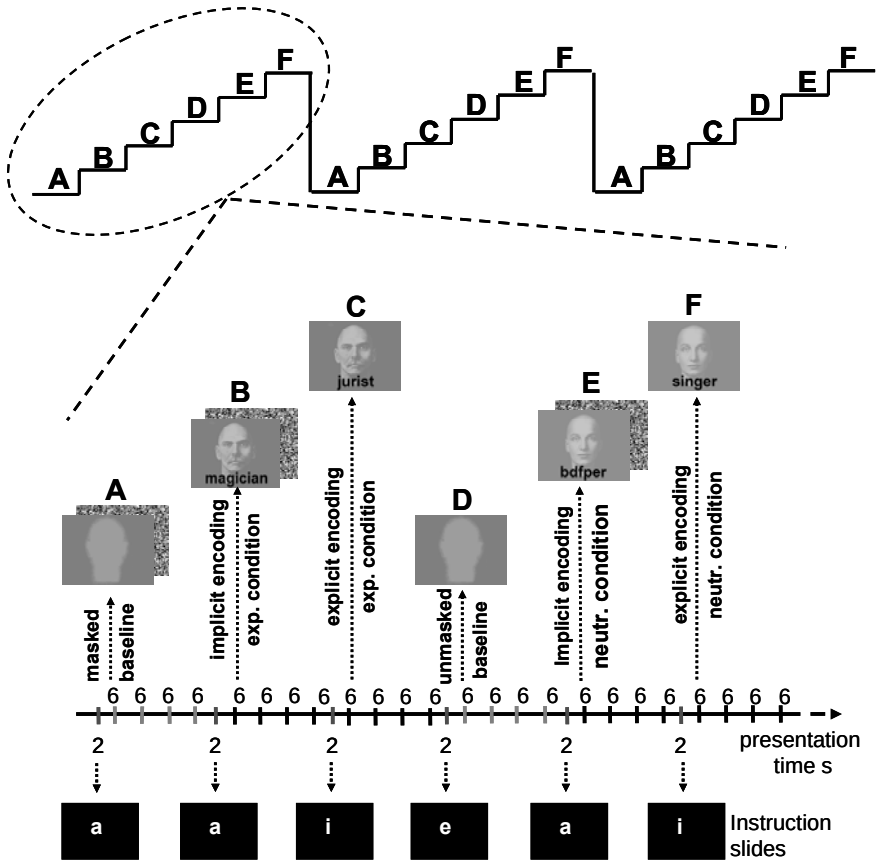

Figure 12. Design of encoding time series.

The instructed strategy for explicit learning (C, F) was to imagine the presented person in a typical scene of the indicated profession. In the masked baseline condition (A) a single head contour was repeatedly presented. Participants were instructed to engage in an attention task during all blocks with masked presentation (A, B, D). In the unmasked baseline condition (D) a series of different head contours was presented for subjects to decide whether the left or right ear of each head contour was larger. There were three blocks, i.e. 12 stimuli per condition. Instruction slides with the letter “i” (imagining a scene) “a” (attentional task) or “e” (ear size) were presented for 2s before each block, to indicate which task has to be perfomed in the following block of 24 s.

The design of the retrieval fMRI time-series was the same in all three experiments. Each retrieval time series consisted of blocks of three different conditions (see Figure 13). The three conditions were a baseline task, retrieval of the experimental condition, and retrieval of the neutral condition. The explicitly learned faces from the experimental and neutral conditions of the encoding scans were presented again as retrieval cues (without professions), four per block, for the subjects to remember the explicitly learned professions. Subjects indicated by button press what professional category each retrieved profession belonged to (academic or artist?). The baseline condition was identical to the unmasked baseline condition used during the encoding scans. There were three blocks, i.e. 12 stimuli, per condition. Instruction slides with the letter “r” (retrieve the profession) or “e” (ear size) were presented for 2s before each block, to indicate which task has to be perfomed in the following block of 24 s.

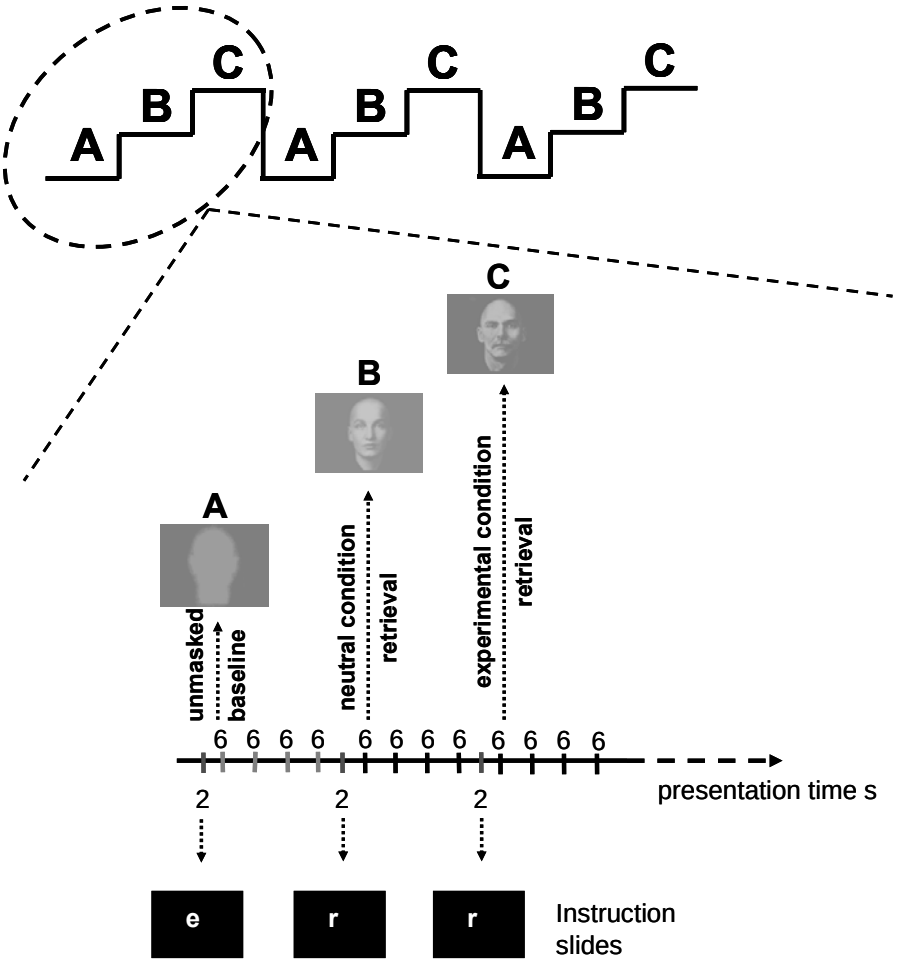

Figure 13. Design of retrieval time series.

Following the retrieval task in all experiments an additional task was done, to test whether the subliminal stimuli had been presented below the objective awareness threshold. For this purpose participants remained situated in the dark scanner. They were exposed to another 30 subliminal face-profession pairs. The masked presentation of each face-profession pair was immediately followed by two forced choice-tasks. One forced-choice task was between the target and a distracter face ("Which face had been subliminally presented?") and the other was between the two professional categories "academic" and "artist" ("Which professional category did the subliminal profession belong to?"; Figure 14). Participants had to answer each of the two forced-choice tasks within 3s by button press.

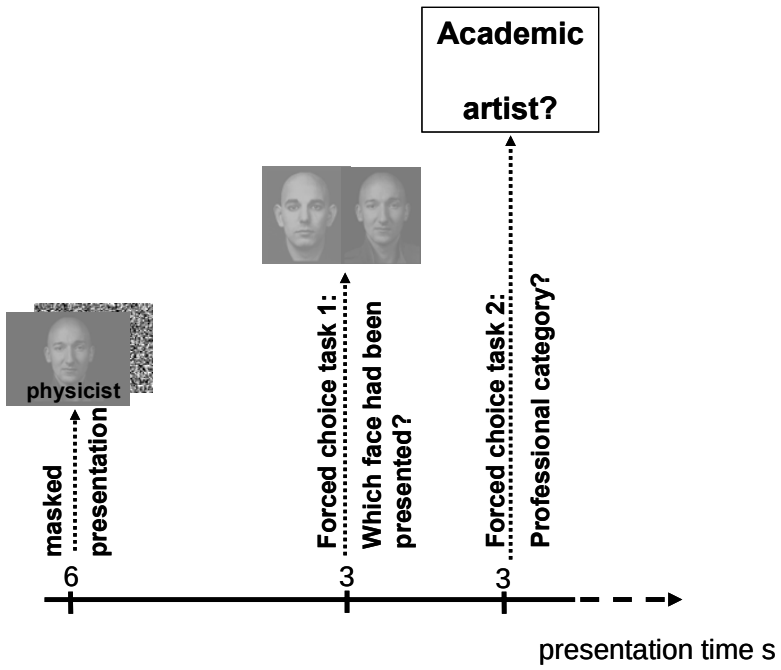

Figure 14. Design of the task that was used to test whether the subliminal stimuli had been presented below the objectively defined awareness threshold. Shown is one trial. In total participants were presented with thirty different target faces and performed two forced choice tasks for each of them. In total 60 new different faces (30 target faces and 30 distracter faces) that never had been presented during the encoding and the retrieval time series had been used.

4.2.4 Behavioural pilot studies

Behavioural pilot studies we conducted previous to our main experiments without imaging, indicated that we should be able to demonstrate modifying effects of implicit learning on subsequent explicit associative learning (Pröll, 2002). However, in the pilot studies the masked presentation of one face-profession pair was always followed immediately by the supraliminal presentation of the corresponding face-profession pair. We used this trial-by-trial design to maximize potential effects of implicit on explicit associative learning. In our pilot experiments we were able to demonstrate that implicitly formed conflicting face-profession associations affected subsequent explicit learning and reduced retrieval performance significantly to a degree of about 50%. However, we were not able to demonstrate a facilitating effect of implicitly formed face-profession associations on subsequent explicit learning and retrieval of the identical face-profession pairs. Indeed, we observed a non-significant tendency that the masked presentation of face-profession pairs rather inhibited than facilitated later explicit learning of identical face-profession pairs. We assumed that visual and conceptual priming effects might have been stronger than the implicit formation of semantic face-profession associations. Priming has been observed to interact competitively with explicit learning (Wagner et al., 2000). As already noted, we used semantically congruent but perceptually distinct professional words in the main experiment to exclude perceptual priming effects. Yet, with our design we could not exclude conceptual/semantic priming effects. (An additional fMRI experiment, in which identical stimuli were presented for implicit and explicit learning, was included later on advise of an external reviewer (for details see manuscript)).

As described previously, we presented the stimuli in blocks of four face-profession pairs in the main experiment, i.e. we used a blocked design instead of a trial-by-trial design. Therefore, a modifying effect of implicit on explicit learning and retrieval will only be observed if each subliminally presented face had been linked to its profession. We hypothesised that the effects of this semantic associative learning would be stronger than semantic priming effects.

4.2.5 Participants

Each of the experiments (Experiment 1 – incongruent, Experiment 2 – congruent, Experiment 3 – identical, and Control experiment) had been carried out in a different group of participants. Furthermore, subjects that had participated in the behavioural pilot study or in one of the studies of Henke and colleagues that used similar stimuli were excluded from participation to be sure that all participants were presented with unknown stimuli during the encoding task.

All participants were normally sighted male students without any reported current or past neurological or psychiatric events. Inclusion criterion was a retrieval performance of 8 of 12 face-profession associations in the neutral condition of each experiment. Based on this criterion, we included 16 right-handed men out of 26 in experiment 1 (age: mean 24, SD 2.4, range 21 – 29), 15 right-handed men out of 26 in experiment 2 (age: mean 24.4, SD 2.55, range 21 – 29), 15 right-handed men out of 24 in experiment 3 (all right-handed; age: mean 24.1, SD 2.4, range 20 – 29), and 9 men (6 right-handed, 1 left-handed, 2 ambidexters) out of 18 in the behavioral control experiment (age: mean 25, SD 2.1, range 23 – 29).

4.3 Methods: Technical aspects concerning fMRI

Imaging techniques provide an excellent possibility to investigate which brain areas are involved in performing a certain task in normal humans. Before the new imaging techniques such as fMRI (Figure 15) or PET had been developed, the only possibility to investigate brain structures was to study brain damaged patients or experimentally lesioned animals.

A disadvantage of lesion studies is that they rather demonstrate which processes the brain can perform without the damaged structure than which processes depend on the damaged structures. Yet, the development of new and more potent methods for image acquisition and data analysis enables the use of fairly elaborated experimental designs allowing to isolate certain processing demands experimentally and revealing the underlying neural substrates and possibly networks. So, it might be possible to disentangle the proper function of different brain regions step by step.

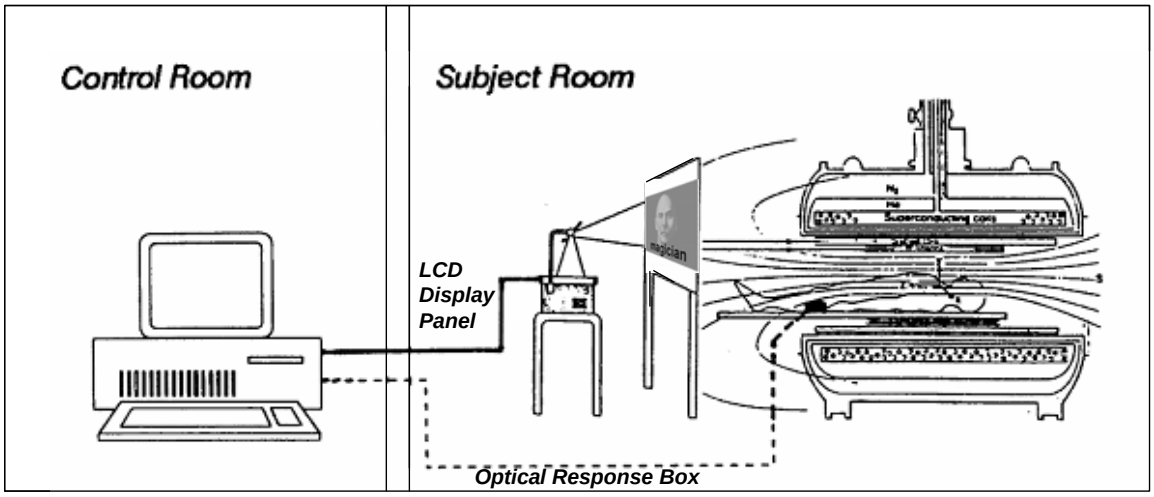

Figure 15. Experimental fMRI set-up. The participant is placed in the MR-scanner and can communicate with the examiner in the control room over a two-way intercom system. The stimuli are presented via LCD projector to the back of a screen the participant watches through a mirror fixated to the head coil. Answers are given by button press via an optical response box that is connected by a glass fibre cable with the computer in the control room.

4.3.1 The BOLD signal

Since 1992, when Ogawa et al. (1992) observed that visual stimulation produces a transient change of the water-proton signal-intensity in the human primary visual cortex that is easily detectable with MRI techniques, many cognitive neuroscientists made use of this fascinating technique. Functional MRI is based on the fact that MRI signal intensity is related to the amount of oxygen that is carried by hemoglobin as oxyhemoglobin and deoxyhemoglobin have distinct magnetic properties. Deoxyhemoglobin is paramagnetic and acts as endogenous contrast agent reflecting the blood oxygen level, i.e. changes in the concentration of deoxyhemoglobin vary the magnetic susceptibility, whereas oxyhemoglobin is diamagnetic and has no effect on the magnetic field.

The local brain oxygen content changes in relation to neural activity. Neural activity is accompanied by both, a local deoxygenation and an increase of tissue perfusion that quickly reverses the deoxygenation and leads to a relative increase in oxygenation that lasts for several seconds (Fox et al., 1988). The decrease in the ratio of deoxy- to oxyhemoglobin causes a detectable increase in proton signal intensity, a

phenomenon Ogawa et al. (1990) termed blood oxygenation-level-dependent (BOLD) contrast.

The BOLD contrast that is used in fMRI offers a powerful, absolutely non-invasive method to measure spatial changes in blood oxygenation in the active brain. Advantages of fMRI compared to positron emission tomography (PET) are the higher spatial and temporal resolution (1-3 mm and 1 or more s in fMRI compared to about 6 mm and 30 s in PET; Friston, 1997), and the possibility to scan participants repeatedly because intrinsic signal changes are measured and therefore no injections of exogenous contrast agents are needed.

4.3.2 How is the BOLD signal related to neural activity?

Although the physical basis of the BOLD signal, as briefly described above, was clear and the robust empirical relationship between changes in brain activity and blood flow had been detected over a century ago (for a review see Raichle, 1998), the questions about the biological mechanisms underlying the BOLD contrast, and the quantitative relationship between neural activity and the BOLD signal are still not answered in conclusion.

A major step ahead in understanding the biological mechanisms underlying the BOLD signal was done by Logothetis and colleagues (2001; for comments see Bandettini and Ungerleider, 2001; Raichle, 2001). The authors have been able to show that the BOLD contrast indeed directly reflects neural responses elicited by a stimulus, and that BOLD signal and neural activity are linearly correlated for short stimulus presentation durations. In their experiments they recorded simultaneously electrophysiological signals and fMRI responses in anaesthetised monkeys that were viewing checkerboard patterns. With their special electrical recording techniques, they have been able to distinguish between action potentials (AP) and local field potentials (LFP). Action potentials are the all-or-nothing responses of firing neurons or neuron groups and occur immediately after stimulus presentation. Local field potentials are more slowly varying electrical potentials reflecting changes of the field potential arising from the incoming input to and the local processing within ensembles of neurons. The heamodynamic response correlated much better with the LFPs than with more direct measures for APs and seems therefore to reflect the incoming input and the local processing, i.e. the pre- and postsynaptic processing in a specific area

rather than spiking activity of efferent neurons (for reviews see Lauritzen and Gold, 2003; Logothetis, 2003).

Though cognitive neuroscientists can be confident that the changes of the BOLD signal really do represent changes in neuronal activity, the biological mechanisms underlying the blood flow increase, i.e. the coupling of vascular and metabolic responses and neuronal activity are still a matter of debate. It seems obvious that the blood flow increase is somehow related to the increased metabolic demands of active neurons. The oxidative metabolism of glucose is one way to supply the brain with energy. Surprisingly, it had been observed in PET (Fox and Raichle, 1986; Fox et al., 1988) and fMRI (Kim and Ugurbil, 1997) studies that neural activity increased glucose uptake and blood flow much more than oxygen consumption. This leads to a relative increase of oxygen level in active brain areas that can be measured with the BOLD contrast. Further, it can be concluded from these data that the brain gains a part of the needed energy via glycolysis, a rapid process of breaking down glucose anaerobically and that is the preferred process to gain energy in astrocytes. Recent data provide an attractive explanation for the BOLD signal assigning a central role to astrocytes in coupling neuronal activity with energy metabolism (Magistretti and Pellerin, 1999). The hottest candidate for triggering both, the vascular and the metabolic responses is the neurotransmitter glutamate (Bonvento et al., 2002; Zonta et al., 2003). The majority of the neuronal information is transmitted via the fast excitatory glutamate-mediated system 80-90% of the cortical synapses are glutamatergic. Here a simplified version of the proposed model explaining how brain microcirculation could be controlled by Glutamate: Glutamate is released from axonal terminals during synaptic activity and diffuses to glutamate receptors located in astrocyte membranes at the border of the synaptic cleft. The activation of the glutamate receptors triggers a change of the Ca2+ concentration in astrocyte processes spreading to the endfeet that are in contact with arterioles, where the changes of Ca2+ concentration regulate the release of vasoactive agents from the asctrocyte endfeets. The release of vasoactive agents leads to a dilation of the arterioles and to an increased blood flow (Zonta et al., 2003).

However, the signalling pathway that enables the regulation of glucose consumption according to increasing needs during neuronal activity is still unknown. Since glucose oxidation by glutamatergic neurons was calculated to be 75-80% compared to about 10% by GABAergic neurons (Rothman et al., 1999), it seems to be very probable that

glutamate plays also a major role in triggering the metabolic response. Currently discussed is the role of glutamate transporters that regulate the glutamate uptake of astrocytes, where glutamate is recycled to glutamin. The increase of glutamate levels in astrocytes leads to an increase in glucose utilization and lactate production (Pellerin and Magistretti, 1994). However, the energetic requirements of glutamate uptake into and recycling in astrocytes are too small, to account completely for the observed changes in glucose metabolism.

4.3.3 Why using a block design in fMRI?

The MRI signal increases about 2 seconds after the stimulus onset (i.e. after neural activity begins) and reaches a plateau after about 7 to 10 seconds. The signal remains elevated while the activity continues and returns to baseline after about 8 to 11 seconds when activity ends. Experience has shown that presenting stimuli of the same condition in blocks of about 20-25 seconds induces a quite stable BOLD response (Figure 16).

Because signal changes induced by subliminally presented stimuli are presumably more difficult to detect than signal changes induced by stimuli that are consciously processed, we decided to use a blocked design.

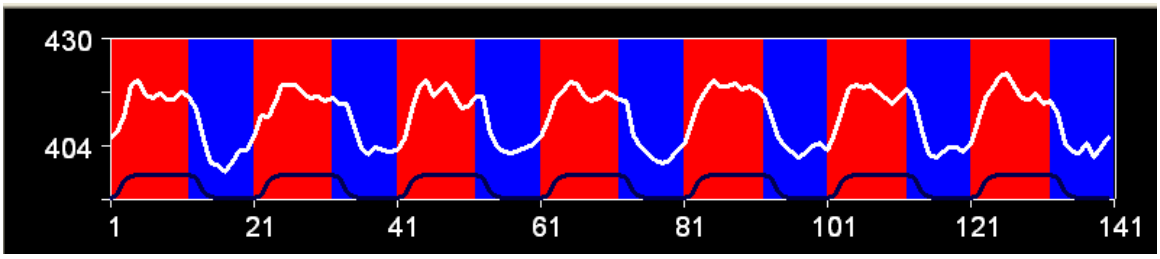

Figure 16. The BOLD signal changes in a block design. The red colour bars refer to blocks of the experimental condition and the blue colour bars refer to blocks of the baseline condition. The white graph shows the experimentally measured BOLD signal changes over the time course of the experiment whereas the black graph illustrates the estimated signal changes. (Picture with courtesy of Martina Schacher, Swiss Epilepsy-Center, unpublished data).

A further advantage of the block design is, that a relatively small number of stimuli are sufficient to induce signal changes that can be detected. This is of crucial importance in our study for two reasons. First, because we want to induce decreases as well as improvements of the recall performance, the retrieval performance in the neutral condition (where explicit learning has not been influenced by previous implicitly formed incongruent or congruent associations) has to be above chance but not too close to the maximal performance level. Thus, we required that participants reach a medium retrieval performance to prevent potential effects of implicitly formed semantic associations being masked by ceiling or floor effects. Second, we did not want to repeat the time series for learning to improve the retrieval performance, because we assumed that potential modifying effects of implicit learning on subsequent explicit learning and retrieval might be masked by the presumably stronger effects of repeated explicit learning. Therefore, participants should be able to reach the learning criterion after one time series for learning. For these reasons, we were restricted to the use of a relatively small number of stimuli.

Of course, the use of a blocked design brings also disadvantages. For example, we will not be able to isolate trials of implicit learning that had a modifying effect on subsequent explicit encoding and retrieval from trials where the effects of implicit learning on explicit learning had been to weak to induce a modification. Newer fMRI methods, such as event-related designs would provide this possibility. In event-related designs the signal changes of one single event are analyzed. However, because one single event induces only small blood flow changes, a relatively large number of comparable events is needed to reach enough statistical power and to be able to detect the signal changes. Because we are restricted to the use of a relatively small number of stimuli for an adequate learning and retrieval performance, the use of an event-related design was not an option. We therefore decided to use the more stable blocked design and loose the possibility to isolate different trials.

4.4 Results

4.4.1 Results at a glance

In the following section the results will be summarised very briefly. A more detailed report and discussion of the results is included in the manuscript of the study. Some additional data figures that are not included in the manuscript are presented in the Appendix (chapter 9).

Our behavioural data provide additional evidence that new semantic associations can be established in the absence of conscious awareness for the learning episode and even the learning material. Furthermore, implicitly formed semantic associations modified subsequent explicit learning and retrieval of both, semantically congruent (experiments 2 and 3, congruent and identical) and incongruent (experiment 1) associations. The neural network mediating the modifying effect involved the hippocampal formation in all experiments.

As hypothesised, implicitly formed associations hindered subsequent explicit learning of incongruent semantic associations and reduced retrieval performance to a degree of about 50%. Furthermore, participants reported significantly more often difficulties to perform the explicit encoding task in blocks following the subliminal presentation of conflicting face-profession pairs, compared to explicit learning blocks following the masked presentation of face-nonword pairs (no implicit semantic associations could be formed).

However, we did not observe a facilitating effect of implicitly formed semantic associations on subsequent explicit encoding and retrieval of semantically congruent or associations. Unexpectedly, the subliminal presentation of face-profession pairs impaired also subsequent explicit encoding and retrieval of semantically congruent associations. Retrieval performance was reduced significantly by implicitly formed semantic associations to a degree of about 50% when semantically congruent face-profession pairs had to be learned explicitly. In the third experiment, retrieval performance had been reduced to a degree of about 30% by previously implicitly formed identical face-profession associations. We discuss a possible explanation for this startling observation in our manuscript.

5 Manuscript:

Implicit associative learning engages the hippocampus and interacts with explicit associative learning

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Abbreviated title: Implicit Learning Interacts with Explicit Learning

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Summary

The hippocampus is crucial for conscious, explicit memory but it is uncertain whether it is also involved in nonconscious, implicit memory. Here we investigated whether the implicit learning of face - profession pairs influenced the explicit learning of face - profession pairs using functional magnetic resonance imaging. The presentation of subliminal face-profession pairs for implicit learning was followed by the explicit learning of supraliminal pairs composed of the same faces combined with professions semantically incongruous to those presented subliminally (experiment 1), semantically congruous professions (experiment 2) or identical professions (experiment 3). We found that implicit paired-associate learning interacted with explicit learning in all experiments impairing explicit retrieval. Hippocampal signal changes from subliminal face-nonword pairs to subliminal face-profession pairs were significant and correlated with the impairment of explicit face-profession retrieval. Our findings extend previous views on memory because they suggest that implicit one-trial paired-associate semantic learning is possible, engages the hippocampus and influences later explicit learning/retrieval.

Introduction

Long-term memory has been subdivided into hippocampus-dependent memories, known as declarative or explicit memories, and hippocampus-independent memories, known as nondeclarative or implicit memories (Graf and Schacter, 1985; Squire, 1992a, 1992b; Squire and Zola-Morgan, 1991). While the formation and retrieval of declarative memories is associated with conscious perception and retrieval of the learning material, nondeclarative memories are incidentally formed and reactivated without conscious awareness of retrieval. This distinction between hippocampus-dependent and hippocampus-independent memory systems along the dimension of awareness is based on findings from patients with hippocampal damage. These patients have deficits on explicit memory tests in spite of normal or near-normal performance on implicit memory tests (Cohen and Squire, 1980; Corkin, 1968; Milner et al., 1968; Warrington and Weiskrantz, 1968). The existence of these hypothesized memory systems has also been supported by several functional neuroimaging studies in healthy human volunteers (for review see Cabeza and Nyberg, 2000; Schacter and Buckner, 1998).

For explicit memory, it is well established that the rapid formation and retrieval of new associations is mediated by the hippocampus and related cortices (Cohen and Eichenbaum, 1993; Davachi et al., 2003; Henke et al., 1997, 1999; Lepage et al., 2000; Mayes et al., 1998; Montaldi et al., 1998; Rolls and Treves, 1998; Small et al., 2001; Sperling et al., 2001; Wallenstein et al., 1998). For implicit memory, doubts have been raised as to whether the rapid formation and retrieval of new associations is possible without conscious awareness (Bowers and Schacter, 1990; Schacter, 1998; McKone and Slee, 1997; Musen and Squire, 1993; Schacter and Buckner, 1998; Squire, 1992a). However, new functional neuroimaging studies in healthy volunteers (Henke et al., 2003a, 2003b; McIntosh et al., 2003; Rose et al., 2002; Schendan et al., 2003) and new behavioral findings in amnesic patients with hippocampal damage (Chun and Phelps, 1999; Curran, 1997; Rajaram and Coslett, 2000a; 2000b; Savage et al., 2002; Yang et al., 2003) suggest that rapid associative learning and retrieval may occur without conscious awareness and engage the hippocampus and parahippocampal gyrus. For example, Yang et al. (2003) examined priming for new word-word and color-word associations by use of a perceptual identification task in eighteen patients with lesions in the medial temporal lobe. In contrast to control subjects, and despite a normal level of single item priming,

these patients failed to show superior identification of old versus recombined word-word or color-word pairs. This finding is in line with the results of our previous neuroimaging experiment on implicit associative learning and retrieval in healthy volunteers (Henke et al., 2003b). We have subliminally presented faces with written professions for implicit associative learning (experimental condition) and faces alone for implicit single item learning (control condition). Although participants were unaware of the subliminal stimuli, activity in the hippocampus and perirhinal cortex changed from the experimental (associative) to the control (single item) condition. These activity changes correlated with the reaction time measure of the later nonconscious retrieval of the face-profession associations. For retrieval, the previously presented faces were shown above threshold with the instruction to guess the professional category of each person (to implicitly reactivate previously formed face-profession associations). Activity in the hippocampus and perirhinal cortex was enhanced when subjects were confronted with faces that had been presented with professions versus faces that had been presented alone. The degree of these hippocampal and perirhinal activity changes correlated with the reaction time measure of nonconscious retrieval. Both studies suggest that medial temporal lobe structures are involved in implicit relational memory. Nevertheless, the representational status of the implicitly formed associations in these studies remained unclear. While compositionality and representational flexibility have been considered key features of explicitly formed associations (Cohen and Eichenbaum, 1993; Dienes and Berry, 1997; Squire, 1992a), there is as yet little experimental evidence (e.g., Greene et al., 2001) for such representational qualities in implicitly formed associations.

In the current functional magnetic resonance imaging (fMRI) experiments, we investigated whether the implicit learning of twelve face - written profession pairs influenced the explicit learning of twelve face - written profession pairs using functional magnetic resonance imaging. Given the previous evidence indicating that the hippocampus is involved in both implicit and explicit associative learning, we hypothesized that the two forms of learning would interact and that the hippocampus would be involved in this interaction. The presentation of twelve subliminal face-profession pairs for implicit learning was followed by the explicit learning of twelve supraliminal pairs composed of the same faces combined with professions semantically incongruous to those presented subliminally (experiment 1),

semantically congruous professions (experiment 2) or identical professions (experiment 3). We hypothesized that the effects of implicit on explicit learning would be facilitatory or inhibitory, depending on whether the implicitly learned information was semantically congruous or incongruous to the explicitly learned information. Each fMRI experiment was conducted with a separate subject group. Experiment 1 contained the semantically incongruous condition. Subliminal face-profession pairs were flashed for 17 ms, preceded and followed by pattern masks, for subjects to implicitly process and store the faces and written professions as paired-associates. This subliminal presentation was followed by supraliminal (6 s, no masks) presentations of the same faces which were now combined with new, semantically incongruous professions to those previously flashed (e.g., implicit learning: face A with ‘magician’; explicit learning: face A with ‘jurist’; Figure 1A). In experiment 2, which contained the semantically congruous condition, the subliminal face-profession pairs were followed by supraliminal presentations of the same faces combined with new, semantically congruous professions (e.g., implicit learning: face A with ‘lawyer’; explicit learning: face A with ‘jurist’; Figure 1A). Experiment 3 contained the identical condition in which the same face–profession pairs were presented subliminally and supraliminally (e.g., implicit learning: face A with ‘jurist’; explicit learning: face A with ‘jurist’; Figure 1A).

The three experiments also included a neutral condition which the experimental condition (congruous, incongruous or identical) was compared to. For the neutral condition, twelve subliminal faces were presented in combination with nonwords (e.g. bdfper) that do not contain lexical-semantic information and hence exclude the linking of lexical-semantic information to faces. Therefore, the subsequent explicit learning of the same faces in association with first-time presentations of written professions remained uninfluenced by previously associated occupational knowledge. It should be noted that effects of face priming and visual or phonological associative priming were present in both the experimental and the neutral condition of all experiments and thus got subtracted out in the comparisons. The component of interest in these studies was implicit *semantic* paired-associate learning. The three experiments also included a subliminal and a supraliminal baseline condition, where single head contours (no physiognomy) were presented either with or without masks. The instructed strategy for explicit learning was to

imagine the presented person in a scene of the indicated profession. This task automatically induces the semantic binding of the profession to the face.

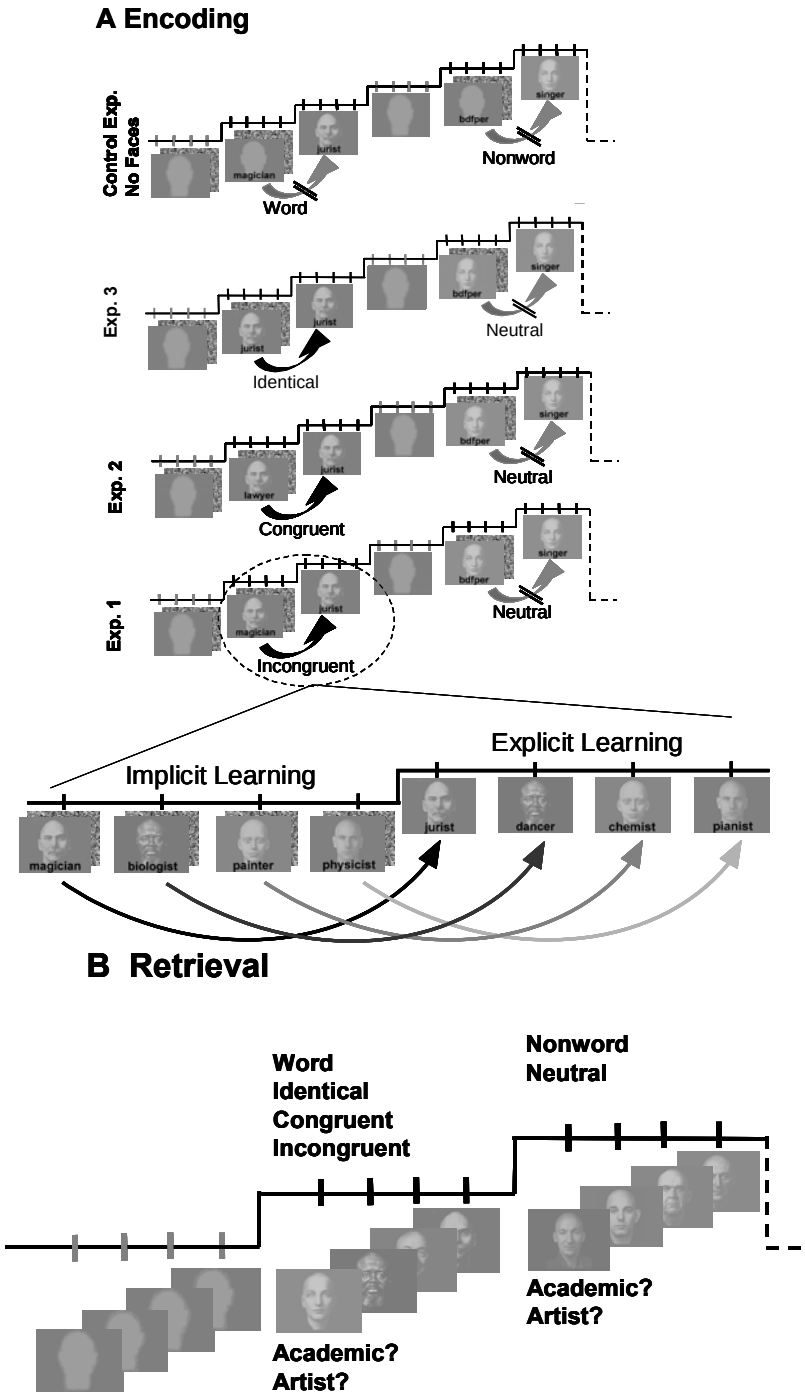

Figure 1. Experimental Design. (A) Encoding fMRI time-series. In the experimental conditions of experiment 1, 2 and 3, each block of four supraliminal face-profession pairs was preceded by a block of masked presentations of the same four faces (A, lower part). These masked faces were either combined with professions that were semantically

incongruent to the later presented supraliminal professions (experiment 1) or combined with professions that were semantically congruent to the later presented supraliminal professions (experiment 2) or combined with the same professions that were later supraliminally presented for explicit learning (experiment 3). In the neutral conditions of experiment 1, 2 and 3, each block of four supraliminal face-profession pairs was preceded by a block of masked presentations of the same four faces combined with nonwords. The instructed strategy for explicit learning was to imagine the presented person in a scene of the indicated profession. In the masked baseline condition a single head contour was repeatedly presented. In the unmasked baseline condition a series of different head contours was presented for subjects to decide whether the left or right ear of each head contour was larger. There were three blocks per condition (the figure illustrates just one task cycle). The behavioral control experiment was identical to experiment 1, except that the subliminal professions and nonwords were presented along with a head contour (always the same head contour) in place of faces. Note that the original professions were written in German. (B) Retrieval fMRI time-series. The design of the retrieval fMRI time-series was the same in all experiments. The explicitly learned faces from the experimental and neutral conditions of the encoding scans were presented again as retrieval cues (without professions), four per block, for the recall of the explicitly learned professions. Subjects indicated by button press the professional category (academic or artist?) for each face. The baseline condition was identical to the unmasked baseline condition used during the encoding scans. Faces are reproduced from the book *"Heads"* (1985) by permission of A. Kayser.

A fourth, purely behavioral experiment (behavioral control experiment) was conducted with an independent subject group to test for implicit effects of masked written professions alone on explicit face-profession learning. The behavioral control experiment was identical to experiment 1, except that the subliminal professions (experimental condition) and nonwords (neutral condition) were presented along with a head contour (always the same head contour) in place of faces.

To exclude the confounding effects of concurrent explicit on implicit stimulus processing, stimuli given for implicit learning were presented below the objectively defined awareness threshold (Cheesman and Merikle, 1984) with a visual backward masking paradigm (Henke et al., 2003b). Masking methods render stimuli invisible to the conscious mind by interrupting neural responses to masked stimuli (Kovacs et al., 1995; Rolls and Tovee, 1994). To ensure a constantly high level of attention throughout subliminal presentations and the direction of the subject's gaze at the eye level of the subliminal faces, we had subjects engage in a visual detection task

during masked presentations. A fixation cross, which was sometimes replaced by a vertical or horizontal bar, was briefly interjected between masks once per second at a location which corresponded to the midpoint between the eyes of the subliminal faces. The task was to detect and indicate by button press the presence of a horizontal or vertical bar. The delay between the presentation of each subliminal stimulus and its corresponding supraliminal stimulus was 18 s in all experiments. This constant delay was achieved by using a block design. A block of four subliminal stimuli was always followed by the block which contained the four corresponding supraliminal stimuli presented in the same order (Figure 1A).

Explicit retrieval was tested minutes after the presentation of the learning trials. The design of the retrieval tasks was the same in all experiments. The explicitly learned faces from the experimental and neutral conditions were presented again as retrieval cues (without professions) with the instruction to remember the (explicitly) associated professions and to indicate which professional category - academic or artist - a retrieved profession belonged to (e.g., “pianist” ⇨ “artist”). This semantic translation ensured that semantic rather than non-semantic face-profession associations were being retrieved (Figure 1B).

Results

Behavioral Data

Visual Detection Task

Accuracy (percent correct) in detecting the flashed horizontal and vertical bars did not differ significantly between the three masked conditions in either of the experiments (ANOVA; all $p>0.3$). Neither did accuracy differ significantly between the four experiments with data pooled over masked conditions (ANOVA; $F_{(3, 51)} = 1.909$, $p = 0.14$; M/SEM % correct; experiment 1: 93.6%/0.87%; experiment 2: 93.5%/1.3%; experiment 3: 94.8%/1.24%; behavioral control experiment: 90.1%/1.9%).

Encoding

The instruction for explicit learning of the face-profession pairs was to imagine the presented person in a scene of the indicated profession. In experiment 1 and the behavioral control experiment, subjects were instructed to indicate by button press

for each face-profession pair whether they were able to imagine a scene or not. This instruction was changed in the subsequent experiments 2 and 3. Here, subjects were instructed to indicate by button press for each face-profession pair whether they found it easy or hard to imagine a scene. Consequently, behavioral measures of explicit encoding were the percentage of imagined scenes (experiment 1 and behavioral control experiment) or the percentage of easily imagined scenes (experiment 2 and 3) as well as reaction latencies for these responses.

fMRI Experiments 1, 2 and 3. An ANOVA with the factors "condition" (experimental vs. neutral condition) and "experiment" (experiment 1, 2, 3) and the dependent variable "percentage of (easily) imagined scenes" revealed no significant main effect for "condition" but a significant interaction ($F_{(2, 40)} = 3.54$, $p = 0.038$; three subjects excluded from this analysis because of incorrect use of response buttons in the imagination task) (Figure 2). Pairwise comparisons showed that imagining a scene was neither statistically different in the congruent condition (M = 64.7%, SEM = 3.2%) compared to the neutral condition (M = 60.3%, SEM = 4.8%; $t_{(12)} = 1.0$, $p = 0.34$) of experiment 2, nor statistically different in the identical condition (M = 56.11%, SEM = 3.7%) compared to the neutral condition (M = 51.11, SEM = 4.6%; $t_{(14)} = 1.03$, $p = 0.32$) of experiment 3. However, imagining a scene was harder in the incongruent condition (M = 80.6%, SEM = 4.9%) versus the neutral condition (M = 90.0%, SEM = 3.2%; $t_{(14)} = -2.5$, $p = 0.026$) of experiment 1 (Figure 2). No significant differences appeared in the ANOVA with the reaction times as dependent variable; nor did reaction times significantly differ between conditions of either experiment.

Behavioral Control Experiment. There was no statistical difference in the "percentage of imagined scenes" between the experimental (M = 86.4%, SEM = 6.5%) and the neutral condition (M = 84.3%, SEM = 5.3%) ($t_{(8)} = 0.62$, $p = 0.55$; Figure 2). There were no significant differences in the reaction time data between conditions.

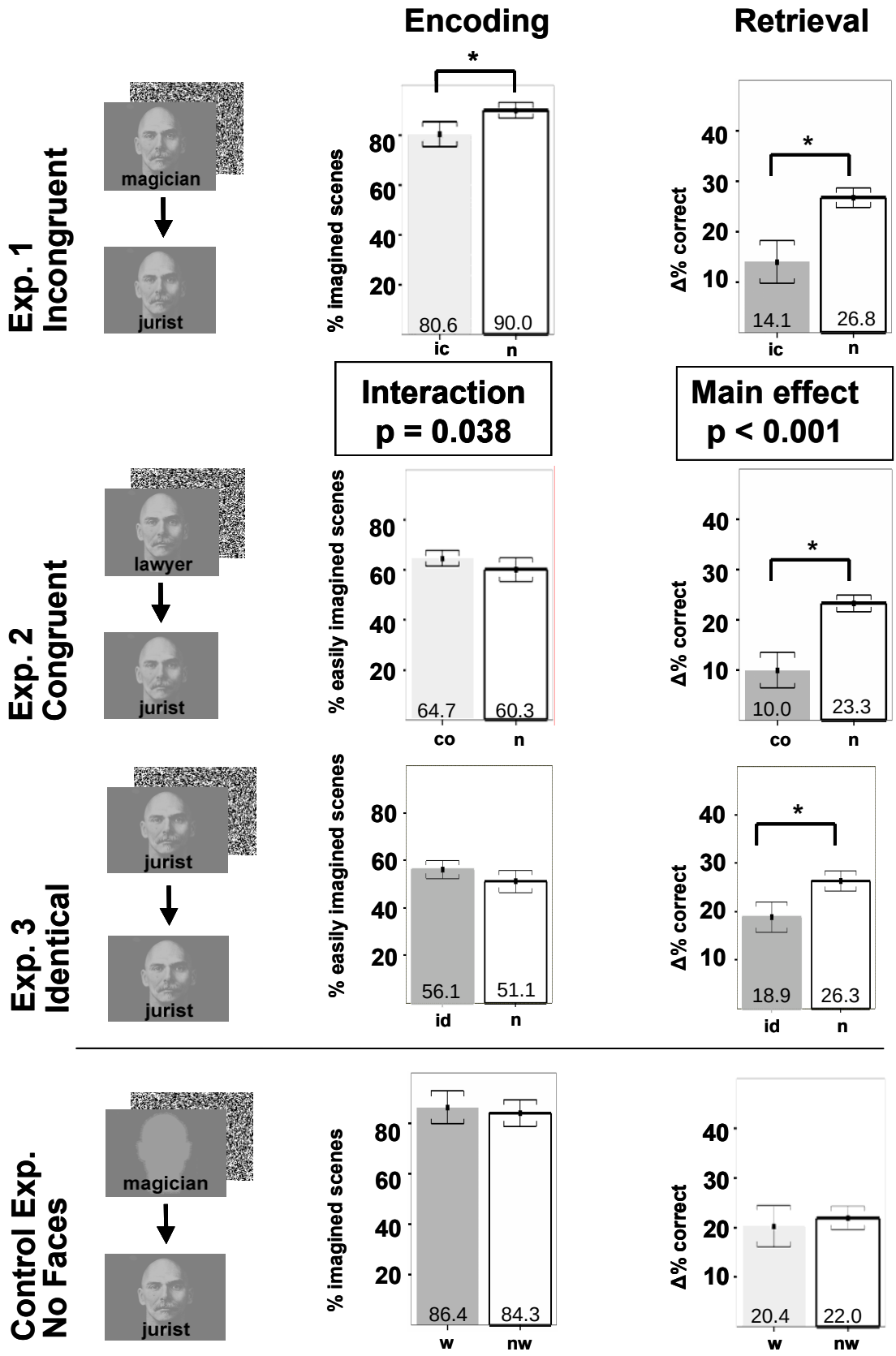

Figure 2. Behavioral Data. The behavioral performance is indicated in means and standard errors of means for the explicit encoding tasks (instruction: “Imagine the presented person in a scene of the indicated profession”) and for the cued recall of the explicitly learned

professions (instruction: “Remember the learned profession and indicate its category, academic or artist, for each face”). The encoding performance is indicated as the percentage of successfully imagined scenes (experiment 1 and behavioral control experiment) or as the percentage of scenes that could be imagined with ease (experiment 2 and 3). The retrieval performance is indicated as the percentage of correctly selected professional categories above chance (50%) level. The icons to the left of the figure illustrate the implicit (with mask) and the subsequent explicit (without a mask) encoding during the experimental condition of each experiment. Ic, incongruent condition; n, neutral condition; co, congruent condition; id, identical condition; w, a word (profession) had been subliminally presented along with a face contour; nw, a nonword had been subliminally presented along with a face contour. Faces are reproduced from the book *“Heads”* (1985) by permission of A. Kayser.

5.1 Retrieval

The retrieval instruction was to remember the (explicitly) associated profession and to indicate by button press which professional category – academic or artist – the retrieved profession belonged to. The performance measure was the percentage of correctly retrieved professional categories minus 50% (50% = chance level).

Experiment 1, 2 and 3. An ANOVA with the factors “condition” (experimental vs. neutral condition) and “experiment” (1, 2, 3) and the dependent variable ”percentage of correctly retrieved professional categories minus 50%” revealed a significant main effect ($F_{(1,\ 43)} = 30.19$, $p < 0.001$) for “condition” (Figure 2), but no significant interaction and no significant main effect for “experiment”. Pairwise comparisons confirmed that retrieval performance was significantly reduced in the experimental condition versus the neutral condition of each fMRI experiment (experiment 1: incongruent M = 14.1%, SEM = 4.2%, neutral M = 26.8%, SEM = 1.9%, $T_{(15)} = -3.12$, $p = 0.007$; experiment 2: congruent M = 10.0%, SEM = 3.5%, neutral M = 23.3%, SEM = 1.7%, $T_{(14)} = -3.46$, $p = 0.004$; experiment 3: identical: M = 18.9%, SEM = 3.2%, neutral M = 26.3%, SEM = 2.1, $T_{(14)} = -3.32$, $p = 0.005$). Consequently, recall performance was reduced by a mean of 47% in the incongruent versus the neutral condition of experiment 1, by a mean of 57% in the congruent versus the neutral condition of experiment 2, and by a mean of 28 % in the identical versus the neutral condition of experiment 3 (Figure 2). No significant differences appeared in the ANOVA with the reaction times for correct answers as dependent variable; nor did

reaction times for correct answers significantly differ between conditions of either experiment.

Behavioral Control Experiment. There was no difference in ”percentage of correctly retrieved professional categories minus 50%” between the neutral (M = 22.0%, SEM = 2.4%) and the experimental condition (M = 20.4%, SEM = 4.2%; $t_{(8)} = -0.26$, p = 0.8; Figure 2). No significant differences appeared in the reaction times for correct answers between conditions.

Test of the Visual Presentation Threshold

Following the experiment, subjects underwent a structured interview about the visibility of the subliminal faces and words and a step-by-step debriefing while still situated in the dark MR scanner. None of the subjects reported to have become aware of features of the subliminal stimuli or to have suspected subliminal presentations during the visual detection task. We can therefore assume that the subliminal stimuli were presented below the subjective awareness threshold (Cheesman and Merikle, 1984). The subliminal presentation mode used in the present studies was adopted from Henke et al. (2003b) where it had been used in other experimental subjects with normal visual acuity. To ascertain that the stimuli were presented below the objective, and not only the subjective, awareness threshold (Cheesman and Merikle, 1984), subjects underwent a forced-choice visibility test at the end of the session. Forty-two of the 46 subjects who had participated in the three fMRI experiments performed this visibility test (visibility data could not be collected in three subjects of experiment 1 and one subject of experiment 2). The visibility test was carried out after the experiments to leave subjects ignorant of subliminal presentations during the experiments and to test their visual discrimination accuracy at the point of maximal visual practice. This visibility test was thus given at a time when subjects had gained the best visual expertise. Moreover, contrary to the fMRI experiment where the subliminal stimuli had been presented in blocks of four followed by the supraliminal presentations, each subliminal stimulus was immediately followed by the forced-choice visibility test. Thus, possible conscious perceptual experiences of masked stimuli might have been likely captured by this trial-by-trial test procedure. However, if there are no measurable effects of conscious stimulus perception immediately after subliminal

presentations, then it appears unlikely that such effects were present after a whole block of subliminal stimuli. Importantly, all psychophysical variables remained constant between the experiment and this test run. Subjects were exposed to another 30 subliminal face-profession pairs which were different from the pairs that subjects had been presented to during the experiment. The masked presentation of each face-profession pair was immediately followed by two forced-choice tasks. One forced-choice task was between the target and a distracter face ("Which of two faces has been subliminally presented?" answers by button press) and the other was between the two professional categories "academic" and "artist" ("Which professional category does the subliminal profession belong to?" answers by button press). In half the trials the face decision was first, counter-balanced across subjects. The order of trials with face decision first or profession decision first was random. The percentage of correct answers of these 42 subjects was not significantly different from chance performance (= 50%) for either face decisions (M = 49.32%, SEM = 1.86; $t_{(41)} = -0.366$; $p = 0.72$) or profession decisions (M = 50.29%, SEM = 1.11%; $t_{(41)} = 0.26$; $p = 0.8$) indicating that subjects were unable to discern visual features or derive word meanings. Because subliminal stimuli of the behavioral control experiment had consisted of a head contour (no faces) and a written profession (Figure 1A) in the experimental condition, we used another thirty head contour-profession pairs for this group's final test run. Hence, their forced choice was only between the two professional categories "academic" and "artist". Subjects' percentages of correct answers indicated chance performance (M = 53.5%, SEM = 2.3%; $t_{(7)} = 1.548$; $p = .166$) suggesting that they were unable to grasp word meanings.

To ensure that no stimulus or selection bias had contributed to these results, we examined face and profession selections, uninfluenced by subliminal faces and words, in 20 further students. Subliminal presentations consisted of a uniform grey screen. Subjects neither selected the target faces (M = 51.75%, SEM = 2.1%; $t_{(19)} = 0.84$, $p = 0.41$) nor professional categories (M = 51.65%, SEM = 2.3%; $t_{(19)} = 0.73$, $p = 0.48$) with a better than chance (50%) accuracy. This suggests that there was no stimulus or response bias which might have masked a potential visibility effect.

Of the two forced-choice tests used, the semantic test which assesses the visibility of the written professions was the critical measure because the effects in the fMRI experiments had originated in the processing of the subliminal words. We therefore looked at each subject's performance in the semantic (profession) forced-

choice test comparing it to the one-tailed 5% cut-off (= 66.66% or 20/30 correct choices) of the chance distribution of correct choices in this test. None of our subjects exceeded this cut-off. We therefore conclude that the masked stimuli were presented below the objective awareness threshold (Cheesman and Merikle, 1984).

Neuroimaging Data

All data were thresholded at $p = 0.001$. We also included activity peaks of $p < 0.01$ if they were located in the brain area of interest (medial temporal lobe) and indicate this lower threshold where applicable.

Implicit Encoding Contrast

Brain activity underlying implicit word reading and the implicit formation of semantic face-profession associations was revealed by comparing the masked presentation of face-profession pairs (incongruent, congruent or identical condition) to the masked presentation of face-nonword pairs (neutral condition) for each experiment (second level contrasts) (Table 1).

Experiment 1 (incongruent). This comparison yielded significance in the right anterior hippocampus/perirhinal cortex ($p<0.01$; Figure 3), left inferior frontal gyrus (Brodmann area, BA, 45), bilateral medial frontal gyri (BA 9 and 10), left lingual/fusiform gyrus (BA 37), left posterior fusiform gyrus (BA 19), right lingual gyrus (BA 18/19), bilateral cuneus (BA 18) and the right caudate nucleus. The reversed comparison revealed an area of significant signal change in the left anterior hippocampus and, at the lower threshold ($p<0.01$), also in the right hippocampus. Further activity changes were located in the left precentral gyrus (BA 6) and the right thalamus.

Experiment 2 (congruent). This comparison revealed activity peaks in the right (Figure 3) and left ($p<0.01$) hippocampus, right temporal pole (BA 38), right postcentral gyrus (BA 1) and right fusiform gyrus (BA 37). The reversed comparison showed activity peaks in the right perirhinal cortex ($p<0.01$), right parahippocampal cortex ($p<0.01$) and right superior temporal gyrus (BA 22).

Experiment 3 (identical). This comparison yielded activity in the right and left (Figure 3) anterior hippocampus, right amygdala, bilateral superior temporal sulci and gyri (BA 22), right middle temporal gyrus (BA 21), left temporal insula, right middle and superior frontal gyri (BA 6, 8), bilateral precentral gyrus (BA 4), bilateral cingulated gyrus (BA 24, 31), left inferior (BA 40) and left superior (BA 7) parietal lobule, right lingual gyrus (BA 18), left cuneus (BA 18), right globus pallidus, right thalamus and left putamen. The reversed comparison revealed no significant activity.

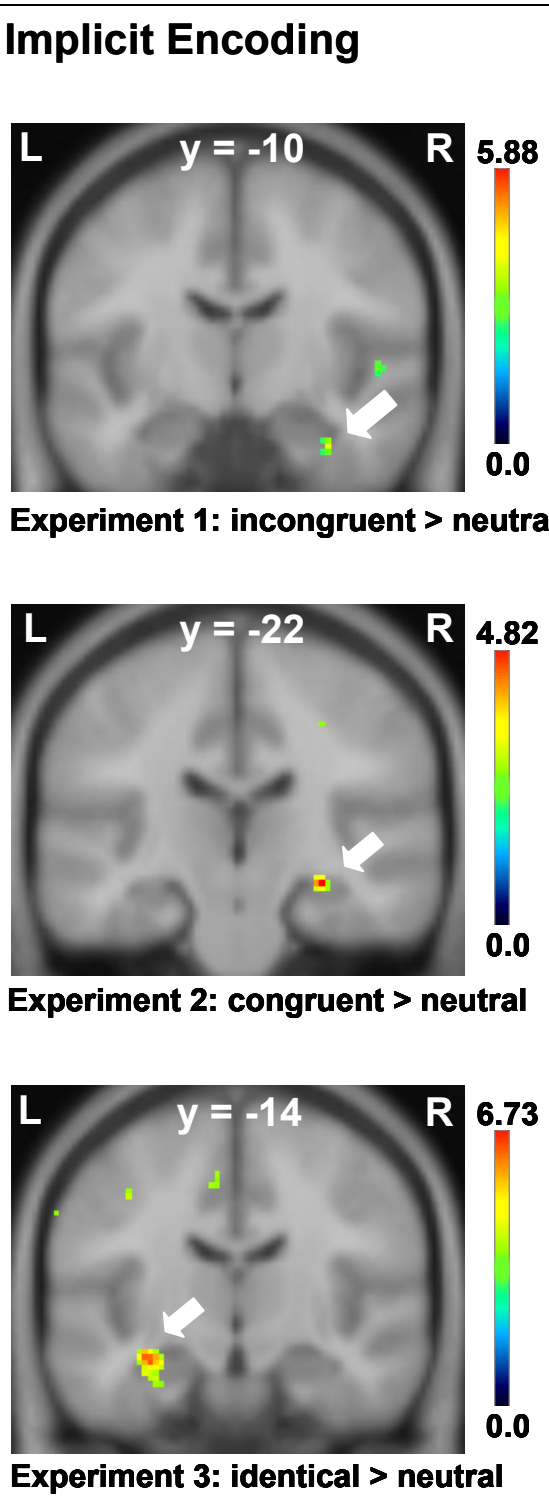

Figure 3. Implicit Encoding Contrast. Hippocampal effects (arrows) resulting from the comparison of the fMRI data in the experimental versus the neutral implicit encoding condition are shown for each fMRI experiment. Differences are illustrated by color-coded t-values (see bar) and presented on coronal sections of the T1-weighted MNI-template of SPM. The anterior-posterior location of each section is indicated by the y MNI coordinate. L, left side of brain; R, right side of brain.

Table 1. Implicit Encoding Contrast

Brain Region	Left/Right	BA [a]	MNI Coordinates (mm) x	y	z	T [b]
One Sample T-Tests						
Experiment 1: Incongruent						
Incongruent > Neutral						
Hippocampus/perirhinal cortex	R		34	-10	-28	4.0*
Inferior frontal gyrus	L	45	-34	32	6	5.34
Medial frontal gyrus	R	9	8	58	18	4.03
Medial frontal gyrus	L	10	-4	54	6	3.99
Lingual/fusiform gyrus	L	37	-18	-52	-14	5.88
Lingual gyrus	R	18/19	6	-66	4	4.71
Fusiform gyrus	L	19	-22	-90	-4	5.07
Cuneus	L	18	-16	-86	22	4.14
Cuneus	R	18	8	-86	26	4.40
Caudate nucleus	R		18	6	16	4.79
Incongruent < Neutral						
Hippocampus	L		-28	-18	-12	5.08
Hippocampus	R		34	-26	-14	3.1*
Precentral gyrus	L	6	-34	4	36	4.27
Thalamus	R		14	-16	14	4.17
Experiment 2: Congruent						
Congruent > Neutral						
Hippocampus	R		30	-22	-12	4.82
Hippocampus	R		36	-32	-12	3.4*
Hippocampus	L		-20	-12	-14	3.7*
Hippocampus	L		-30	-26	-14	2.7*
Temporal pole	R	38	46	12	-30	4.07
Postcentral gyrus	R	1	60	-14	12	4.19
Fusiform gyrus	R	37	38	-54	-26	4.56
Congruent < Neutral						
Perirhinal cortex	R		28	-4	-34	3.4*
Parahippocampal cortex	R	35	24	-42	-2	3.0*
Superior temporal gyrus	R	22	46	-44	16	4.44
Experiment 3: Identical						
Identical > Neutral						
Hippocampus	L		-30	-14	-18	6.15
Hippocampus	R		30	-8	-18	4.73
Amygdala	R		20	-2	-16	5.22
Superior temporal sulcus	R		62	-44	10	5.68
Superior temporal sulcus	R		48	-30	-4	4.98
Superior temporal sulcus	L		-48	-30	-4	3.97
Superior temporal sulcus	L		-64	-48	6	4.50
Superior temporal gyrus	L	22	-62	0	0	4.22
Superior temporal gyrus	R	22	56	-48	20	4.05
Middle temporal gyrus	R	21	40	-68	18	4.45
Temporal insula	L		-34	-20	0	5.46
Middle frontal gyrus	R	6	36	10	44	5.03
Superior frontal gyrus	R	6	12	-6	66	5.22
Superior frontal gyrus	R	8	16	44	42	5.00
Precentral gyrus	L	4	-40	-20	34	4.72
Precentral gyrus	R	4	54	-10	16	4.66
Cingulate gyrus/paracentral lobule	L	31/5	-16	-26	46	6.44
Cingulate gyrus	R	24	6	-8	38	5.14
Inferior parietal lobule	L	40	-48	-28	22	4.24
Superior parietal lobule	L	7	-30	-44	50	4.27
Lingual gyrus	R	18	14	-76	-10	4.84
Cuneus	L	18	-8	-94	24	4.38
Globus pallidus	R		14	-28	12	4.96
Thalamus	R		24	-20	8	6.73
Putamen	L		-26	-24	2	4.13
Identical < Neutral						
No significant difference						

[a] BA, Brodmann Area; [b] T values of peaks within significantly activated clusters of voxels ($p < 0.001$); * ($p < 0.01$)

Correlations between Implicit Encoding Contrast (Experimental – Neutral Condition) and Retrieval Impairment (Recall Neutral – Experimental Condition)

We computed correlations for each experiment between the individual implicit encoding contrasts (experimental – neutral condition) and the later retrieval impairment in the experimental condition. The retrieval impairment was expressed as % correct profession selections in the neutral condition minus experimental condition. The degree of the retrieval impairment is a strong measure of the impact that implicit associative learning had on explicit associative learning. Because the following brain areas are involved in this correlation, they can be considered key areas associated with the interaction between implicit and explicit associative learning (Table 2). Positive correlations imply that the larger the activity enhancement during implicit word reading and implicit associative learning was, the larger the explicit retrieval impairment in the experimental condition.

Experiment 1 (incongruent). Peaks of significant positive correlations were located in the left (Figure 4) and right anterior hippocampus, left superior temporal gyrus (BA 22), left inferior frontal gyrus (BA 45), bilateral middle frontal gyri (BA 10, 6, 46) and left medial frontal gyrus (BA 8). Significantly negative correlations were found in the left uncus (BA 34), right insular cortex and right caudate nucleus.

Experiment 2 (congruent). Peaks of significant positive correlations were situated in the left anterior hippocampus (Figure 4), left amygdala and left inferior frontal gyrus (BA 47).

Significantly negative correlations were located in the right and left ($p<0.01$) anterior hippocampus, bilateral superior temporal sulci, left inferior temporal gyrus (BA 20) and right superior frontal gyrus (BA 6).

Experiment 3 (identical). Peaks of significant positive correlations were situated in the left superior temporal sulcus, right middle frontal gyrus (BA 46), right inferior parietal lobule (BA 40), bilateral precuneus (BA 7) and left cingulate gyrus (BA 23). Significantly negative correlations were found in the right anterior subiculum/hippocampus (Figure 4), left inferior temporal sulcus and left middle frontal gyrus (BA 6).

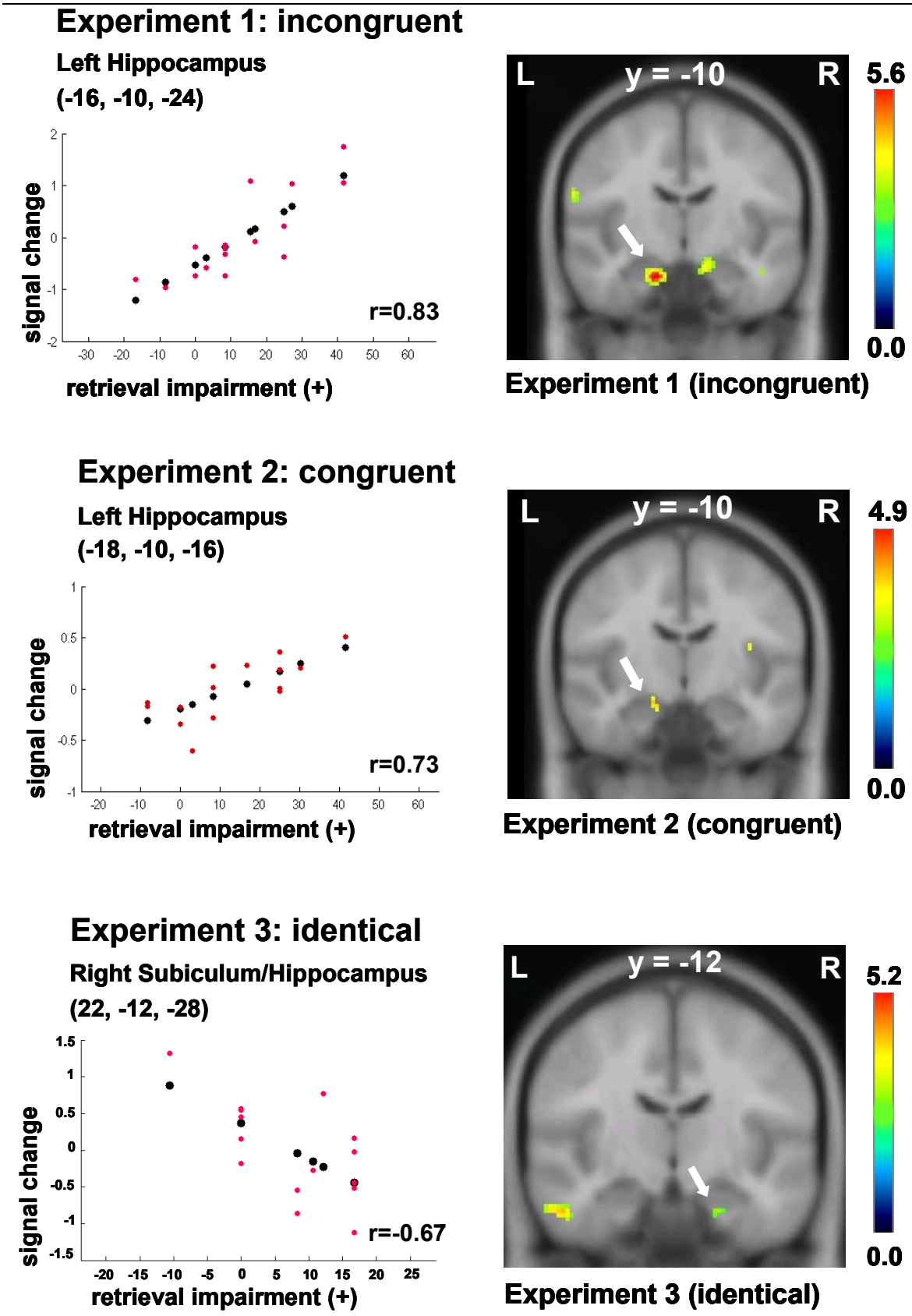

Figure 4. Correlations Between the Implicit Encoding Contrast (Experimental – Neutral Condition) and Retrieval Impairment (Recall Neutral – Experimental Condition). Correlations were computed between the individual implicit encoding contrasts (experimental – neutral condition: masked face-profession pairs versus masked face-nonword pairs) and the later

retrieval impairment expressed as % correctly retrieved professional categories in the neutral condition minus the experimental condition (i.e., positive values stand for retrieval impairment in the experimental condition). The correlation results in the hippocampus (arrows) are shown for each fMRI experiment in scatter plots and as color-coded t-values superimposed on coronal sections of the T1-weighted MNI-template of SPM. The locations of correlation peaks are indicated by MNI coordinates. L, left side of brain; R, right side of brain.

Table 2. Correlations between Implicit Encoding Contrast (Experimental - Neutral Condition) and Retrieval Impairment (Recall Neutral - Experimental Condition)

			MNI Coordinates (mm)			
Brain Region	**Left/Right**	**BA [a]**	**x**	**y**	**z**	**T [b]**
CORRELATION ANALYSIS						
Experiment 1: Incongruent						
Positive Correlations						
Hippocampus	L		-16	-10	-24	5.57
Hippocampus/amygdala	R		12	-8	-18	4.21
Hippocampus	R		30	-22	-12	4.12
Superior temporal gyrus	L	22	-48	-50	26	4.10
Inferior frontal gyrus	L	45	-44	30	8	3.80
Middle frontal gyrus	R	46	40	48	18	4.13
Middle frontal gyrus	R	6	24	0	48	4.13
Middle frontal gyrus	L	10	-40	46	-6	3.98
Medial frontal gyrus	L	8	-8	36	34	4.36
Negative Correlations						
Uncus	L	34	-22	6	-28	3.90
Temporal insula	R		38	-16	14	3.80
Caudate Nucleus	R		12	4	14	3.80
Experiment 2: Congruent						
Positive Correlations						
Hippocampus	L		-18	-10	-16	3.87
Amygdala	L		-14	-8	-20	3.99
Inferior frontal gyrus	L	47	-26	20	-10	4.12
Negative Correlations						
Hippocampus	R		34	-18	-18	4.33
Hippocampus	L		-30	-22	-14	3.2*
Superior temporal sulcus	L		-58	0	-10	3.87
Superior temporal sulcus	L		-60	-10	-12	4.35
Superior temporal sulcus	R		66	-14	-8	4.42
Inferior temporal gyrus	L	20	-48	-30	-18	4.54
Superior frontal gyrus	R	6	20	-10	64	4.10
Experiment 3: Identical						
Positive Correlations						
Superior temporal sulcus	L		-54	-42	8	6.32
Middle frontal gyrus	R	46	34	42	20	4.84
Inferior parietal lobule	R	40	54	-46	36	5.17
Precuneus	L	7	-12	-58	52	5.02
Precuneus	L	7	-8	-44	50	4.69
Precuneus	L	7	-14	-68	36	4.03
Precuneus	R	7	12	-74	48	4.26
Cingulate gyrus	L	23	-6	-16	30	9.71
Negative Correlations						
Subiculum/hippocampus	R		22	-12	-28	3.02*
Inferior temporal sulcus	L		-52	-12	-28	4.24
Middle frontal gyrus	L	6	-30	18	62	5.01

[a] BA, Brodmann Area; [b] T values of peaks within significantly activated clusters of voxels ($p < 0.001$); * ($p < 0.01$)

Correlations between Implicit Encoding Contrast (Experimental – Neutral Condition) and Explicit Encoding Facilitation (% [easily] Imagined Scenes Experimental – Neutral Condition)

We computed correlations for each experiment between the individual implicit encoding contrasts (experimental – neutral condition) and the explicit encoding facilitation expressed as the difference in the percentage of (easily) imagined scenes between the experimental and the neutral condition. This correlation shows in how far and what direction implicit encoding activity relates to the ability to imagine the same person (as subliminally presented) act in a scene of the same (experiment 3) or different profession (experiments 1 and 2) (Table 3). Positive correlations imply that the larger the activity enhancement during implicit word reading and implicit associative learning was, the easier the imagery task.

Experiment 1 (incongruent). Peaks of significant positive correlations were found in the left parahippocampal cortex (BA 35), left inferior temporal gyrus (BA 37), left inferior frontal gyrus (BA 9), left superior parietal lobule (BA 7) and left postcentral gyrus (BA 7). Significantly negative correlations were situated in the right temporal insula, right inferior temporal gyrus (BA 20), left superior temporal sulcus, right superior temporal gyrus (BA 22), left superior frontal gyrus (BA 6), right superior parietal lobule (BA 7), left intraparietal sulcus (BA 7), bilateral postcentral gyrus (BA 2) and right precentral gyrus (BA 4).

Experiment 2 (congruent). Peaks of significant positive correlations were located in the right superior parietal lobule (BA 7), right retrosplenial cortex (BA 30) and right brain stem.

There were no significant negative correlations.

Experiment 3 (identical). Peaks of significant positive correlations were found in the left and right hippocampus, right entorhinal cortex, left parahippocampal cortex (BA 35), right middle frontal gyrus (BA 6), left superior parietal lobule (BA 7), right fusiform gyrus (BA 36, 19), left inferior occipital gyrus (BA 19). Significantly negative correlations were located in the left superior temporal sulcus, right superior temporal gyrus (BA 22) and right anterior cingulate gyrus (BA 32).

Table 3. Correlations between Implicit Encoding Contrast (Experimental - Neutral Condition) and Explicit Encoding Facilitation (% [easily] Imagined Scenes Experimental - Neutral Condition)

			MNI Coordinates (mm)			
Brain Region	**Left/Right**	**BA [a]**	**x**	**y**	**z**	**T [b]**
CORRELATION ANALYSIS						
Experiment 1: Incongruent						
Positive Correlations						
Parahippocampal cortex	L	35	-24	-54	-6	5.59
Inferior temporal gyrus	L	37	-48	-66	-2	5.70
Inferior frontal gyrus	L	9	-38	18	34	4.42
Superior parietal lobule	L	7	-10	-54	64	5.21
Postcentral gyrus	L	7	-10	-46	66	4.54
Negative Correlations						
Temporal insula	R		38	-16	10	5.37
Inferior temporal gyrus	R	20	50	-30	-22	5.43
Superior temporal sulcus	L		-62	-24	-4	4.68
Superior temporal sulcus	L		-56	-40	8	4.68
Superior temporal gyrus	R	22	66	-18	10	4.86
Superior frontal gyrus	L	6	-4	-18	50	4.73
Superior parietal lobule	R	7	22	-58	70	4.33
Intraparietal sulcus	L	7	-34	-42	50	4.24
Postcentral gyrus	R	2	48	-20	20	6.12
Postcentral gyrus	L	2	-46	-28	58	5.86
Precentral gyrus	R	4	52	-6	10	4.83
Experiment 2: Congruent						
Positive Correlations						
Superior parietal lobule	R	7	26	-68	58	5.24
Retrosplenial cortex	R	30	14	-54	16	4.61
Brain stem	R		4	-28	-30	5.14
Negative Correlations						
No significant difference						
Experiment 3: Identical						
Positive Correlations						
Entorhinal cortex	R		22	-26	-22	6.57
Parahippocampal cortex	L	35	-28	-44	-6	6.40
Hippocampus	L		-18	-36	2	4.36
Hippocampus	L		-24	-26	-14	4.34
Hippocampus	R		36	-30	-6	3.7*
Middle frontal gyrus	R	6	38	12	54	4.87
Superior parietal lobule	L	7	-36	-52	50	4.46
Fusiform gyrus	R	36	26	-36	-30	5.84
Fusiform gyrus	R	19	36	-74	-24	4.23
Inferior occipital gyrus	L	19	-42	-90	2	4.84
Negative Correlations						
Superior temporal sulcus	L		-52	-6	-10	5.00
Superior temporal gyrus	R	22	66	-34	10	4.58
Anterior cingulate	R	32	14	44	4	4.89

[a] BA, Brodmann Area; [b] T values of peaks within significantly activated clusters of voxels ($p < 0.001$); * ($p < 0.01$)

Explicit Encoding Contrast

The influence that implicit associative learning had on subsequent explicit associative learning can also be captured in the explicit encoding contrast (experimental condition – neutral condition) (Table 4).

Experiment 1 (incongruent). The explicit encoding contrast yielded significance in the right anterior hippocampus, right parahippocampal cortex, right superior frontal gyrus (BA 9) and left fusiform gyrus (BA 19). The reversed comparison revealed significance in the right inferior temporal gyrus (BA 20, 37) and left precentral gyrus (BA 6).

Experiment 2 (congruent). This comparison revealed significant activity in the right middle temporal gyrus (BA 39), left temporal insula, right superior frontal gyrus (BA 6), right postcentral gyrus (BA 1), right retrosplenial cortex (BA 30), right caudate nucleus and right precuneus (BA 31). The reversed comparison yielded significance in the right anterior hippocampus ($p<0.01$), right perirhinal cortex ($p<0.01$) and right inferior parietal lobule (BA 40).

Experiment 3 (identical). The explicit encoding contrast yielded activity peaks in the right and left ($p<0.01$) perirhinal cortex/hippocampus, right superior temporal gyrus (BA 38), left middle temporal gyrus (BA 21), bilateral inferior frontal gyri (BA 44, 47), right superior frontal gyrus (BA 6) and right precentral gyrus (BA 6), left middle and medial frontal gyri (BA 6), left postcentral gyrus (BA 1), bilateral superior and inferior parietal lobules (BA 7, 40), left globus pallidus and right putamen. The reversed comparison revealed no significance.

Table 4. Explicit Encoding Contrast

			MNI Coordinates (mm)			
Brain Region	**Left/Right**	**BA [a]**	**x**	**y**	**z**	**T [b]**
One Sample T-Tests						
Experiment 1: Incongruent						
Incongruent > Neutral						
Hippocampus	R		32	-12	-22	3.92
Parahippocampal cortex	R		20	-56	0	3.90
Superior frontal gyrus	R	9	24	58	34	4.00
Fusiform gyrus	L	19	-22	-76	-18	4.08
Incongruent < Neutral						
Inferior temporal gyrus	R	20	54	-38	-20	5.72
Inferior temporal gyrus	R	37	62	-56	-18	4.48
Precentral gyrus	L	6	-34	4	30	4.39
Experiment 2: Congruent						
Congruent > Neutral						
Middle temporal gyrus	R	39	44	-66	16	4.55
Temporal insula	L		-30	-22	12	4.06
Superior frontal gyrus	R	6	14	-2	64	3.99
Postcentral gyrus	R	1	44	-20	34	4.82
Retrosplenial cortex	R	30	20	-52	12	5.05
Caudate nucleus	R		22	22	0	4.83
Precuneus	R	31	24	-64	22	4.23
Congruent < Neutral						
Hippocampus	R		38	-14	-22	3.0*
Perirhinal cortex	R		26	-2	-34	2.9*
Inferior parietal lobule	R	40	68	-42	30	4.30
Experiment 3: Identical						
Identical > Neutral						
Perirhinal cortex/hippocampus	R		42	-6	-30	5.39
Perirhinal cortex/hippocampus	L		-28	-8	-30	3.3*
Superior temporal gyrus	R	38	62	12	-2	4.23
Middle temporal gyrus	L	21	-68	-36	0	5.20
Inferior frontal gyrus	R	44	58	10	8	5.22
Inferior frontal gyrus	R	47	42	22	-12	4.54
Inferior frontal gyrus	L	47	-30	18	-10	4.12
Superior frontal gyrus	R	6	12	22	58	4.80
Middle frontal gyrus	L	6	-30	-6	46	4.73
Medial frontal gyrus	L	6	-4	-6	56	4.63
Precentral gyrus	R	6	52	2	38	4.83
Postcentral gyrus	L	1	-66	-12	26	4.43
Superior parietal lobule	R	7	46	-40	64	4.81
Superior parietal lobule	L	7	-38	-54	64	4.76
Inferior parietal lobule	R	40	62	-34	48	4.36
Inferior parietal lobule	L	40	-56	-28	38	4.17
Globus pallidus	L		-16	-26	0	6.14
Putamen	R		24	8	10	5.17
Identical < Neutral						
No significant difference						

[a] BA, Brodmann Area; [b] T values of peaks within significantly activated clusters of voxels ($p < 0.001$); * ($p < 0.01$)

Discussion

We performed three fMRI experiments to investigate interactions between the implicit learning of subliminal face-profession pairs and the subsequent explicit learning of the same faces presented supraliminally combined with either the same profession (experiment 3) or a profession that was semantically incongruous (experiment 1) or semantically congruous (experiment 2) to the subliminal professions. We also performed a behavioral control experiment, where we tested for effects of the subliminal professions alone on the subsequent explicit learning and retrieval of face-profession pairs.

The post-experimental structured interviews about the visibility of the subliminal faces and words showed that no subject had become aware of features of the subliminal stimuli or had suspected subliminal presentations. A post-experimental trial-by-trial forced-choice visibility test confirmed that subjects had no awareness of the subliminal faces and professions. We therefore conclude that the masked stimuli were presented below the objective awareness threshold (Cheesman and Merikle, 1984) of the currently tested experimental subjects. During subliminal presentations, subjects engaged in a visual detection task that directed their gaze at a spot between the eyes of the subliminal faces and ensured a high level of visual attention. Because detection accuracy differed neither between subliminal conditions of experiments nor between experiments, it can be assumed that subjects had fixated gaze and maintained a constantly high level of visual attention. This high level of visual attention may have facilitated the processing of the subliminal information.

Our behavioral data showed that the masked face-profession pairs had influenced explicit learning and had decreased retrieval performance in all experimental conditions. Explicit retrieval performance decreased from the neutral to the experimental condition by a mean of 47% with incongruent professions ($p=0.007$), 57% with congruent professions ($p=0.004$) and 28 % with identical professions ($p=0.005$). The critical implicit process that had generated these effects must have been the implicit formation of semantic face-profession associations for the following reasons. Our experimental conditions allowed for implicit word reading and the implicit associating of words to faces while implicit face processing and implicit visual and phonological paired-associate learning was possible in both the experimental and neutral conditions. Implicit word reading as the only source of the implicit-explicit interaction can be ruled out because the subliminal words alone had

no effect on explicit face-profession learning and retrieval as shown in our behavioral control experiment. This finding is underscored by the behavioral data collected during the explicit learning tasks in the fMRI experiments. The instructed strategy for explicit associative learning was to imagine the presented person in a scene of the supraliminal profession. In comparison to the neutral condition, subjects experienced difficulties imagining individuals in scenes of incongruous supraliminal professions but they had no difficulties imagining individuals in scenes of congruous or identical supraliminal professions. These differential effects at explicit encoding indicate that the interactions had originated in the implicit formation of individual semantic face-profession associations rather than the implicit processing of professions alone. Our finding of one-trial implicit semantic paired-associate learning is important because earlier findings had cast doubts on the feasibility of forming and retrieving associations implicitly within just one trial (Bowers and Schacter, 1990; McKone and Slee, 1997; Musen and Squire, 1993; Squire, 1992a). On the other hand, the current results are consistent with our previous findings suggestive of implicit one-trial semantic paired-associate learning (Henke et al., 2003a, 2003b).

The retrieval impairment in the incongruent condition is likely due to semantic interference between implicitly and explicitly formed associations because subjects experienced difficulties imagining individuals in incongruent professions at the time of explicit encoding. Unsuccessful imagery might have impeded the explicit formation and retrieval of face-profession associations. In addition, the consolidation of two conflicting memory traces, the implicit memory trace A – B and the explicit memory trace A – C, may have weakened memory storage and perhaps added to the retrieval impairment.

The reason for the negative influence that implicit associative learning had on explicit associative learning in the congruent and the identical condition is less clear. When supraliminal professions were congruous or even identical to subliminal professions, imagery remained unaffected. Thus, the subliminal face-profession associations did not interfere with imagery when word semantics were congruous or identical. On the other hand, there was also no significant facilitation of imagery in these conditions. No signs of classic repetition priming were observed during the second encounter with the identical or congruous supraliminal pairs as accuracy and reaction times collected during imagery did not significantly differ between experimental and neutral conditions, nor was explicit encoding associated with a

significant repetition suppression of the BOLD signal as would be expected during the processing of a primed stimulus (Henson, 2003; Schacter and Buckner, 1998). On the contrary, the BOLD signal was enhanced during the congruent and the identical explicit encoding condition versus the neutral explicit encoding condition within the hippocampal area (only identical condition), temporal, frontal and parietal neocortex and basal ganglia. This signal enhancement during explicit encoding may reflect at least two things: the encoding of a greater number of stimulus aspects yielding a better retrieval performance, which was not the case, or increased computational demands at explicit encoding due to competing concurrent processes. The latter interpretation receives support by the correlations which were positive between the explicit encoding contrasts (experimental – neutral condition) and retrieval impairment (data not shown). I.e., the greater the signal enhancement during the explicit encoding of identical or congruous pairs the greater the retrieval impairment. Competition at the time of explicit encoding may emanate from the recovery and comparison of implicit with explicit face-profession pairs. These competing processes possibly interfere with the formation and consolidation of explicit memories. For explicit memory, it is well established that repeated versus once processed supraliminal information leads to an improvement, not an impairment, of retrieval performance (Ebbinghaus, 1885/1992). Hence, in the realm of explicit memory such recovery and comparison processes have no negative effects on the re-encoding and retrieval of information. We therefore assume that the subliminal presentation mode and the lack of awareness of the initial stimulus presentations had reversed the otherwise positive effects of repeated encoding. The reason for this reversal is at present unclear because this is the first study of effects that subliminal stimulus pairs may have on explicit associative learning. It should also be noted that our face-profession learning task was difficult and that our subjects were selected on grounds of their good learning and retrieval performance in the uninfluenced explicit learning situation. It is therefore conceivable that a good associative learning system is well capable of forming associations even implicitly and therefore suffers from greater interference by recovered implicit associations during explicit encoding than a less capable associative learning system would.

It should also be noted that the mean retrieval impairment was larger in the congruent condition (57%), where subliminal and supraliminal professions were different, than in the identical condition (28%), where professions were the same.

Perhaps some degree of semantic interference also applied to the congruent condition, and not only to the incongruent condition.

The fMRI signal recorded during implicit face-profession learning (experimental condition) versus implicit face-nonword learning (neutral condition) was enhanced within the anterior hippocampus in each experiment (Figure 3). Also explicit face-profession learning yielded robust and bilateral anterior hippocampal signal increases in all conditions of all three experiments (data not shown). These results along with previous findings (Chun and Phelps, 1999; Curran, 1997; Henke et al., 2003a, 2003b; McIntosh et al., 2003; Rajaram and Coslett, 2000a, 2000b; Rose et al., 2002; Savage et al., 2002; Schendan et al., 2003; Yang et al., 2003) suggest a role for the hippocampus not only in explicit but also implicit relational learning. Notably, the notion of the hippocampus as a relational processor comes primarily from animal experiments (Cohen and Eichenbaum, 1993; Bunsey and Eichenbaum, 1996; Dusek and Eichenbaum, 1997; Rolls and Treves, 1998) where conscious awareness or autonoetic consciousness (Tulving, 1985) of learning and retrieval is not as much a topic as in the human literature. The animal and human data together may extend the classic views of memory systems which do not posit a role for the hippocampus in implicit memory (Graf and Schacter, 1985; Squire, 1992a, 1992b; Squire and Zola-Morgan, 1991). The contrasts of implicit face-profession learning versus implicit face-nonword learning yielded also enhanced activity in several neocortical areas including temporal and prefrontal cortices known to mediate lexical-semantic analyses necessary for word comprehension. These results vary between the three fMRI experiments even though the contrast isolates equal implicit processes in all three experiments. The likely reason for this variability is not only between-subject variability but perhaps mainly the different imaging protocols used in the three fMRI experiments. All measurements were performed on a 3T Philips Intera whole body system. Yet, the scanner and imaging protocols were improved over the time that these experiments were carried out. We started out with conventional echo-planar imaging in experiment 1 (incongruent), where no lateral temporal activity differences were apparent, and went on to parallel imaging with SENSE (Pruessmann et al., 1999) in experiment 2 (congruent) and 3 (identical), where lateral temporal activity differences became apparent. SENSE reduces image distortions and susceptibility artifacts in the temporal lobes saving signal that can be compared across conditions (Preibisch et al., 2003; Schmidt et al., submitted). Furthermore, experiments 1

(incongruent) and 2 (congruent) were performed with the "Master" gradient system (30mT/m gradient strength, 150mT/m/ms slew rate) while the experiment 3 (identical) was performed with the "Triade" gradient system (80mT/m gradient strength, 100mT/m/ms slew rate). The latter allows for faster data acquisition and therefore enhanced gradient-echo EPI quality. This may explain the many differentially activated areas during implicit learning in experiment 3 versus experiments 1 and 2.

We correlated the individual implicit encoding contrasts (face-profession learning versus face-nonword learning) with the degree of the explicit retrieval impairment for each experiment to reveal the brain areas associated with the interaction between implicit and explicit memory. These correlations yielded significance in the anterior hippocampus in all three experiments (Figure 4). Thus, the degree of the hippocampal engagement in the implicit encoding of face-profession pairs versus face-nonword pairs related to the degree of the explicit retrieval deficit. This result is important because it suggests that the hippocampus was not merely coactivated during masked presentations but changed its engagement relative to the impairing effects that implicit had on explicit memory. The anterior location of the correlation and subtraction results within the hippocampus corresponds to previous evidence of an anterior hippocampal engagement in explicit semantic associative learning (Henke et al., 1997, 1999, 2003a; Schacter and Wagner, 1999; Sperling et al., 2001, 2003). We therefore assume that the anterior part of the hippocampus participates in both the explicit and implicit formation of new semantic associations. Further correlation sites in the three experiments were situated in the left lateral temporal cortex, left inferior frontal gyrus (BA 45 and 47), middle frontal gyrus (BA 46, 10), medial frontal gyrus (BA 8) and superior frontal gyrus (6). These temporal-frontal regions have been found implicated in the semantic processing of verbal and pictorial supraliminal stimuli in previous neuroimaging studies (e.g., Devlin et al., 2002; Grabowski et al., 2001; Martin and Chao, 2001; Perani et al., 1999; Pilgrim et al., 2002; Vandenberghe et al., 1996; Wagner et al., 2001). These correlation results therefore suggest that the better the masked words were understood and semantically related to faces, the more detrimental was their effect on explicit retrieval. This finding underscores our earlier interpretation based on the behavioral results that the effect of implicit on explicit memory originated in the implicit formation of semantic rather than visual or phonological associations between words and faces.

Remarkably, medial temporal activity changes during the masked experimental versus neutral condition were bidirectional (table 1). We have previously observed bidirectional hippocampal signal changes during the masked presentation of face-profession pairs versus masked single items (Henke et al., 2003a, 2003b). We propose the following reason for this phenomenon: During the masked presentation of face-profession pairs, and less during the masked presentation of single items, hippocampal neurons engage both in the spontaneous encoding of the omnipresent conscious thoughts (Stark and Squire, 2001) and the encoding of the masked stimuli. If additional hippocampal neurons to those engaged in the encoding of conscious thoughts turn to encode the masked stimulus pairs as soon as the experimental condition comes up, then activity in the experimental condition rises over the activity in the neutral condition. If, however, those neurons that are engaged in the encoding of conscious thoughts happen to be neurons specialized in the encoding of face-profession pairs, then at least a subgroup of these neurons will stop encoding conscious thoughts and switch over to encoding masked face-profession pairs. This switch will effectively decrease activity in that area during the experimental versus the neutral condition because the evoked neural responses by masked stimuli are interrupted by the masks (Kovacs et al., 1995; Rolls and Tovee, 1994) which likely decreases the BOLD signal. Thus, the balance of implicit and explicit encoding activity in the hippocampus appears to both dependent of the type of masked stimuli (pairs versus single items) and the type and extent of simultaneous conscious mental activity. Although our subjects engaged in the same visual detection task during all masked conditions, they were still free to have additional conscious thoughts. Furthermore, the bidirectional hippocampal signal changes during implicit encoding produced bidirectional correlations between the implicit encoding contrasts and retrieval impairment (table 2).

These and previous findings of implicit relational learning (Henke et al., 2003a, 2003b) may modify the view that conscious awareness be necessary for snapshot associative learning (Bowers and Schacter, 1990; McKone and Slee, 1997; Musen and Squire, 1993; Squire, 1992a). The implicit semantic associations of the present experiments were formed ‘on the fly’, within just one trial. These kinds of rapid associative learning have been considered characteristic of hippocampal learning as opposed to neocortical learning which is viewed as incremental and slow (Norman and O'Reilly, 2003; O'Reilly and Rudy, 2000; Rolls and Treves, 1998). We assume

that rapid semantic associative learning invariably engages the hippocampus, mainly in its anterior aspect, independent of stimulus awareness. The current and earlier results (Greene et al., 2001; Willingham, 1997) may also extend the prevailing view that implicitly formed associations consist of rigid, fused or noncompositional representations while explicitly formed associations are flexible, compositional and allowing for generalization (e.g., Cohen and Eichenbaum, 1993; Dienes and Berry, 1997; Squire, 1992a; but see Cohen et al., 1999). Flexibility and compositionality have been considered key features of hippocampal processing (Cohen and Eichenbaum, 1993; Eichenbaum et al., 1996). For the present argument, it should be kept in mind that the trials in our experiments were given in blocks of four subliminal face-profession pairs, immediately followed by blocks of the four corresponding supraliminal counterparts which were presented in the same order. The delay between each subliminal and its corresponding supraliminal counterpart was 18 s. This design requires that each subliminal face be linked to its profession in a compositional way to make possible the semantic interference that we observed in the incongruent condition: at the time of explicit learning, a face (A) must have been retrieved in isolation to be identified as the common piece of information present in the implicit (**A** – B) and the explicit (**A** – C) stimulus pair. In addition, the implicit association (A – B) must be reactivated and compared in terms of semantic congruency to the explicit association (A – C).

These results have implications for theories of memory systems. The division of hippocampus-dependent and hippocampus-independent memory systems along the dimension of awareness had been motivated by the initial findings of preserved implicit memory skills in hippocampal amnesic patients (Corkin, 1968; Cohen and Squire, 1980; Milner et al., 1968; Warrington and Weiskrantz, 1968). Yet, it may turn out that not every form of implicit learning is independent of the hippocampus.

Experimental Procedures

Subjects

Fifty-five student subjects participated in the four experiments and fulfilled our inclusion criteria. These subjects did not report past or current psychiatric or neurological problems, denied to take drugs or medication, were normally-sighted, male and achieved an above chance retrieval performance in the neutral conditions of the present experiments. We adopted a retrieval criterion of at least 66.66% correct (50% = chance) which corresponds to 8 of 12 correctly retrieved associations in the neutral condition, i.e., the condition which remained uninfluenced by implicit semantic associations. A worse retrieval performance in the neutral condition would not leave room for a potential impairing effect of the subliminal stimuli on explicit learning/retrieval in the experimental condition. Of the 55 subjects who fulfilled these inclusion criteria, 16 participated in experiment 1 (all right-handed; age: mean 24, SD 2.4, range 21 – 29), 15 in experiment 2 (all right-handed; age: mean 24.4, SD 2.55, range 21 – 29), 15 in experiment 3 (all right-handed; age: mean 24.1, SD 2.4, range 20 – 29) and 9 in the behavioral control experiment (6 right-handed, 1 left-handed, 2 ambidexters; age: mean 25, SD 2.1, range 23 – 29). Thus, the four subject groups were well matched in terms of age, gender, education and visual acuity. Moreover, due to our inclusion criterion, all subjects had a rather good explicit learning capacity for the material at hand. Written informed consent was obtained prior to all experiments. Yet, subjects were only informed after the experiments that stimuli had been briefly flashed between masks. The study was approved by the local ethics committee for human studies.

5.2 Procedure

Experiments 1 to 3 consisted of two fMRI time-series with blocked trials, one time-series for encoding and one time-series for retrieval, separated by 5 minutes (Figure 1). The same procedure was applied to the behavioral control experiment which was also conducted in the MR scanner but no MR data were collected. Following interviews and paper work, subjects of all four experiments were situated in the completely darkened MR scanner for the dark adaptation of their eyes, practiced the tasks, went through the experiment, the post-experimental debriefing and finally took the forced-choice tests to evaluate the used presentation threshold.

In both the encoding and the retrieval parts of all experiments, twelve stimuli were presented per condition, divided into three blocks of four trials. Each trial took 6 s: unmasked stimuli were presented during the whole 6 s time window, while masked stimuli were presented 12 times for 17 ms between masks and fixation slides within the 6 s time window. The order of trials per condition and the order of conditions per time-series were varied between subjects. However, each block of four explicit learning trials was always immediately preceded by the block containing the corresponding implicit learning trials. The four stimuli of an implicit learning block were presented in the same order as the corresponding four stimuli presented in the following explicit learning block to ensure a constant delay of 18 s between each subliminal stimulus and its supraliminal counterpart. Stimulus sets used for learning and retrieval were rotated over conditions to distribute stimulus generated effects.

The encoding fMRI time-series of experiments 1 - 3 included an experimental condition with incongruous subliminal and supraliminal professions presented with faces in experiment 1, congruous subliminal and supraliminal professions presented with faces in experiment 2 and identical subliminal and supraliminal professions presented with faces in experiment 3. The encoding fMRI time-series of experiments 1 - 3 also included a neutral condition which the experimental condition was compared to. The neutral condition included subliminal presentations of face-nonword pairs followed by supraliminal presentations of face-profession pairs (Figure 1A; see introduction).

The encoding part of the behavioral control experiment was identical to experiment 1, except that the subliminal professions (experimental condition) and nonwords (neutral condition) were presented along with a head contour (always the same head contour) in place of faces. This manipulation prevented the semantic binding of words to individual faces. It allowed us to investigate effects of the subliminal words alone on subsequent explicit learning.

The encoding part of all four experiments also included an implicit and an explicit baseline condition. The repeated masked presentation of one single head contour (without physiognomy) was used for the implicit baseline condition. Unmasked presentations of different head contours were used for the explicit baseline condition (Figure 1A).

The retrieval part was the same for all four experiments (Figure 1B). The explicitly learned faces from the experimental and neutral encoding conditions were

presented again, unmasked and in a new order, as retrieval cues for the explicit recall of the explicitly learned professions. The retrieval part of all experiments also included a baseline condition which was the same as the explicit baseline condition used for encoding.

Tasks

Implicit Learning

In all experiments, the masked presentations were introduced to subjects as a visual detection task which was indeed the task subjects engaged in while viewing subliminal presentations. Between the sequence of subliminal stimuli and masks, a fixation slide was briefly presented once per second. This black fixation slide contained either a white cross or - in a sixth of presentations - a white horizontal or vertical bar at a location which corresponded to the midpoint between the eyes of the subliminal faces. The task subjects intentionally engaged in was to detect and indicate by button press the occurrence of a horizontal or vertical bar. Blocks of masked presentations were announced by a 2 s presentation of the letter “d” for “detection task”.

Explicit Learning

In order to achieve a comparable encoding quality among subjects, the encoding strategy was instructed in all experiments. It required subjects to imagine each presented person in a scene of the indicated profession. This imagery task automatically induces a semantic processing of the face and the written word as well as a semantic face-word binding. For experiment 1 and the behavioral control experiment, subjects were instructed to indicate by button press whether a scene could be imagined or not. Because this instruction yielded about 90% yes-answers in these initially performed experiments, we changed this instruction for the subsequently performed experiments 2 and 3. The aim of this change was to get a more even response distribution which leaves room for a potential increase in the number of positive responses as an effect of the previously flashed congruous/identical occupational information. The new instruction for experiments 2 and 3 required subjects to indicate by button press whether they found it easy or hard to imagine a presented person in a scene of the indicated profession. Blocks of

explicit learning were announced by a 2 s presentation of the letter “i” for “imagery task”.

In the explicit baseline condition of all experiments, head contours were presented with the instruction to indicate by button press whether the area of the left or the right ear was larger. These task blocks were announced by a 2 s presentation of the letter “e” for “ear task”.

Explicit Retrieval

In all experiments, the faces that had been learned explicitly during the experimental and neutral encoding conditions were presented again during the experimental and neutral retrieval conditions, respectively. The faces acted as cues for the explicit recall of the explicitly learned occupations. The instruction was to recall the associated profession, translate it into the higher professional category – academic or artist – and to indicate the respective professional category by button press.

The baseline condition consisted of the ear task that had already been used as a baseline in the encoding part of experiments.

Stimuli and Masking Paradigm

Stimuli were adopted from Henke et al. (2003b). They consisted of 48 black-and-white full frontal portraits of unknown bald individuals with neutral facial expressions and without paraphernalia (Kayser, 1985). Stimuli were digitized and degraded in contrast for the subliminal presentations; the same low-contrast images were also used for the supraliminal presentations (Figure 1). Ten academic and 10 artistic professions were assigned to faces in equal proportions and in a way that the appearance of individuals was not indicative of the assigned professions. Professions were typed below faces (Figure 1A). The 48 face–profession pairs were divided into 4 sets of 12 stimuli for use in the explicit learning conditions of all experiments (set1-explicit, set2-explicit, set3-explicit, set4-explicit). For implicit learning, three variants of each set were created. For the incongruous implicit condition of experiment 1, faces were combined with a profession of the opposite professional category (e.g., explicit: singer [artist]; implicit: physician [academic]). For the congruous implicit condition of experiment 2, faces were combined with semantically closely related professions from either the same semantic level (e.g., engineer – architect, pianist – organist) or from the subordinate level (e.g., physician – surgeon, singer - soprano).

For the implicit neutral conditions of experiments 1 - 3, faces were combined with nonwords (e.g., bdfper). The nonwords had word lengths comparable to those of the used written professions; although they were pronounceable, they did not sound like German profession words.

For the explicit baseline task used in all experiments, head contours (Figure 1) were created such that the area of either the right or the left ear was larger. In the implicit baseline task used in all experiments, one of these head contours was repeatedly presented. This same head contour was combined with the incongruous professions and nonwords, which had been used in the implicit encoding conditions of experiment 1, for use in the implicit encoding conditions of the behavioral control experiment.

Forty black-and-white visual noise images were adopted from Henke et al. (2003b) and used as masks for the subliminal presentations. The fixation slide, which was repeatedly displayed during the masking sequences for the stabilization of gaze, had a black background with a white cross at a location which corresponded to the midpoint between the eyes of the subliminal faces. The fixation cross was replaced by either a vertical or a horizontal white bar on two further slides which were used for the visual detection task.

We used the masking technique of Henke et al. (2003b). A stimulus (S) was presented 12 times within 6s for 17 ms. Visual noise masks (M) were presented for 183 ms and a fixation cross/vertical/horizontal bar (F) was presented for 233 ms. The stimulation sequence for one trial (6 s) was F - M - S - M - M - S - M - F - M - S - M - M - S - M - F - M - S - M - M - S – M - F - M - S - M - M - S - M - F - M - S - M - M - S - M - F - M - S - M - M - S – M. The subjective perception of this presentation consisted of moving black and white grains interrupted by the fixation cross/bar.

MR Image Acquisition

All measurements were performed on a 3T Philips Intera whole body system. However, experiments 1 and 2 were performed with the "Master" gradient system (30mT/m gradient strength, 150mT/m/ms slew rate), while experiment 3 was performed with the "Triade" gradient system (80mT/m gradient strength, 100mT/m/ms slew rate). The latter allows for faster data acquisition and therefore

enhanced gradient-echo EPI quality in terms of susceptibility artefact reduction and reduced T2*-blurring.

Parameters of Experiment 1

Functional T2*-weighted images were acquired with an echo-planar pulse sequence (EPI) from 32 axial slices covering the whole brain with an acquisition matrix of 80 x 80 (voxel size 2.6 x 2.6 x 4 mm^3) which was reconstructed into an image matrix of 128 x 128 (voxel size 1.6 x 1.6 x 4 mm^3). Acquisition parameters were TR 4500 ms, flip angle 90°, TE 30 ms, no inter-slice gaps.

Parameters of Experiments 2 and 3

We applied the fast imaging technique Sensitivity Encoding (SENSE) (Pruessmann et al., 1999; Weiger et al., 2000; Schmidt et al., submitted) in the second and third experiment using a transmit-receive body coil and a commercial eight-element head coil array (MRI Devices Corporation, Waukesha WI, USA). Parallel imaging techniques like SENSE provide enhanced encoding efficiency which is achieved by using spatially varying coil sensitivity profiles, allowing the reconstruction of under-sampled data. The benefits are a reduction of susceptibility artifacts, distortions and blurring and a substantial increase in spatial resolution (Preibisch et al., 2003; Schmidt et al., submitted). Functional T2*-weighted images were acquired from 32 axial slices covering the whole brain with an acquisition matrix of 80 x 80 (voxel size 2.75 x 2.75 x 4 mm^3) which was reconstructed into an image matrix of 128 x 128 (voxel size 1.7 x 1.7 x 4 mm^3). A SENSE single-shot-echo-planar-imaging (SENSE-sshEPI) readout was applied with a reduction factor of 2.4. Further acquisition parameters were TR = 3000 ms, flip angle 82°, TE = 35 ms, no inter-slice gaps.

MR Image Analysis

Image post-processing and the statistical analyses of all fMRI data were performed using Statistical Parametric Mapping (SPM2; http://www.fil.ion.ucl.ac.uk/spm/). Volumes were realigned to the first volume to remove movement-related variance components (Friston et al., 1995). As a prerequisite for inter-subject averaging, images from all subjects were spatially normalized into standard stereotaxic space (standard EPI template SPM2). Data were smoothed to a full width of 8 mm at half-

maximal resolution using a Gaussian filter to increase signal to noise ratio and to conform data to a Gaussian field model.

Single-Subject Level

The fMRI data of all subjects were analyzed voxel by voxel by modeling the conditions as box car functions convolved with a hemodynamic response function and applying the general linear model (fixed effects model; Cohen, 1997) provided in SPM2 (http://www.fil.ion.ucl.ac.uk/spm/). A high-pass filter with a cut-off period of 128 s was used. The six head movement parameters were included as confounding factors. We computed implicit encoding contrasts (implicit experimental encoding condition versus implicit neutral encoding condition) and explicit encoding contrasts (explicit experimental encoding condition versus explicit neutral encoding condition).

Group Level

The resulting within-subject contrasts of each subject were further analyzed in a second level analysis (SPM2; random effects analysis) to account for the variance between subjects. Signal differences were considered reliable if they exceeded a threshold of $p < 0.001$ (uncorrected); results at the lower significance level of $p<0.01$ were only included if located in the region of interest, the medial temporal lobe.

Correlations between fMRI Signal and Behavioral Measures

For each experiment, we computed correlations between the within-subject implicit encoding contrasts (experimental - neutral condition) and the behavioral measure of the later retrieval impairment as well as the behavioral measure of the explicit encoding facilitation (simple regression, SPM2). The retrieval impairment was expressed as % correct professional categories in the neutral condition minus % correct professional categories in the experimental condition. This subtraction leads to positive numbers for retrieval impairment in the experimental condition. The explicit encoding facilitation was expressed as % (easily) imagined scenes in the experimental condition minus % (easily) imagined scenes in the neutral condition. This subtraction leads to positive numbers for a facilitated explicit encoding in the experimental condition. Signal differences were considered reliable if they exceeded a threshold of $p < 0.001$ (uncorrected); results at the lower significance level of $p<0.01$ were only included if located in the region of interest, the medial temporal lobe.

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6 General discussion

6.1 Support for the relational account

The behavioural data reported in the present study (chapter 5) provides additional evidence for the hypothesis, that new semantic associations can be established in the absence of conscious awareness for the learning episode and the learning material. Furthermore, implicitly formed associations modified subsequent explicit learning and retrieval. Based on our presented results, we conclude that the modifying effect of the subliminally presented face-profession pairs was induced rather by implicitly established links between the faces and the meaning of the profession words than by the masked presentation of the profession words alone. The semantic interaction between implicit and explicit learning in our design depends on the ability to recognize that a specific face had been presented in a different (or similar) semantic context. This means that the observed modifying effect of implicit on explicit learning and retrieval depends critically on the ability to implicitly link the face and the semantic of the profession word as two separate entities composing a related pair rather than as a fused unity. Thus, our findings are additional evidence that implicitly formed associations consist not necessarily of rigid, fused or noncompositional relations.

Moreover, our imaging findings suggest that the hippocampus is part of the neural network mediating the modifying effect of implicit on explicit learning and was also involved in linking the faces and the semantics of the professional words in our implicit learning task. The hippocampus is assumed to be critically involved in the formation and recollection of (flexible) semantic associations (Cohen and Eichenbaum, 1993; Davachi et al., 2003; Henke et al., 1997; Henke et al., 1999; Lepage et al., 2000; Mayes et al., 1998; Montaldi et al., 1998; Rolls and Treves, 1998; Small et al., 2001; Sperling et al., 2001; Wallenstein et al., 1998), whereas the perirhinal cortex is suggested to be involved in single item learning and familiarity based recognition memory (Aggleton and Brown, 1999; Brown and Aggleton, 2001; Davachi et al., 2003). Based on the hypothesis that the hippocampus is involved in the formation of new associations irrespective of the level of awareness, it can be hypothesised that implicitly formed associations are not necessarily rigid and inflexible. Indeed, our behavioural and neuroimaging data suggest that flexible,

hippocampus-dependent memories can be established independent of conscious awareness for the learning episode or even the learning material.

Thus, our results are further evidence supporting the relational account claiming that the hippocampus is involved whenever new (flexible) relations between previously unrelated items are formed irrespective of the level of awareness. This implies that hippocampus-dependent tasks are not necessarily explicit and do not necessarily measure declarative forms of memory. Hence, the involvement of conscious awareness seems not to be a factor that predicts reliably whether task performance depends on the hippocampus or not. Because the declarative/nondeclarative account is based on the assumption that the hippocampus is exclusively involved in declarative memory (Squire, 1992a), the discussed results challenge this account heavily. However, these findings are in agreement with the view supported by the relational account (Cohen et al., 1999; Eichenbaum, 1999). In the relational account a task is assumed to depend on the hippocampus whenever successful performance requires the establishment of new relations, i.e. the hippocampus is suggested to mediate the networking of memory with or without conscious awareness. Thus, the processing demands of the memory task determine its hippocampus-dependency and not the level of awareness involved at encoding or retrieval.

6.2 Arguments against the declarative/nondeclarative account

Whether conscious awareness for the learning episode or the learning material is relevant for success or not is one of the crucial questions to distinguish between different forms of long-term memory in the declarative/nondeclarative as well as in the implicit/explicit account. Main support for the crucial importance of this question came from studies with amnesic patients and lesioned animals. Undoubtedly, the exploration of dissociations between declarative or explicit and nondeclarative or implicit forms of memory in amnesic patients and healthy participants has extended the knowledge about how long-term memory is organised over the past decades. However, there are some concerns about using the level of awareness as distinguishing feature. First, there is still some disagreement about how to define the presence or absence of conscious awareness. Even if the philosophical aspects of this question are neglected, it is still not a trivial question to answer and there have

been several attempts to find pragmatic and satisfying criteria to estimate whether conscious awareness had been involved or not.

In studies with humans the question of whether conscious awareness was involved or not can directly be addressed, i.e. the experimenter can for example ask the participants whether they intentionally retrieved words from the studied list during the word-stem completion part in a priming experiment or not. As discussed earlier, self-reports are not fully reliable, because they depend on memory for prior states of awareness. The observation of neuropsychological phenomena such as "blindsight" (perception of visual stimuli without awareness) in patients with damage to the visual cortex, or nonconscious recognition of familiar faces in patients with "prosopagnosia" (facial-recognition deficits), point towards another potential problem arising from using self-reports to define whether conscious awareness was involved or not. Blindsight refers to a paradoxical phenomenon observed in patients with damages to areas in the primary visual cortex. In an experiment of Weiskrantz and colleagues (1974) such patients denied having seen a stimulus presented in a certain part of the visual field. But when asked to guess about the location or other attributes of the stimulus, their performance was well above chance and sometimes nearly perfect, indicating some form of "sight" despite their subjective impression of blindness. A similar paradoxical form of implicit or nonconscious knowledge has been observed in patients with prosopagnosia. Prosopagnosia refers to the inability to recognize familiar faces usually because of bilateral lesions to occipito-temporal cortex. In a study of Bauer (1984) the patients were presented with faces that were well known to them (e.g. a relative or the spouse), while reading a list of names to them. The patients showed a maximal skin conductance response to the correct name, despite denying any familiarity with the presented face. This finding has been replicated by Tranel and Damasio (1985) using a slightly different paradigm. These neuropsychological phenomena indicate that subjective verbal reports in which participants deny awareness for a stimulus can be in disagreement with their behavioural responses that indicate that there has been some form of perception. Observations like these have put forward the question, whether verbally denying conscious awareness is sufficient to exclude the involvement of conscious awareness (Schacter, 1992).

Cheesman and Merikle (1984) have proposed a pragmatic approach to address this problem. They suggested a distinction between subjective and objective measures of

conscious perception. Subjective measures of conscious perception rely on participants verbal reports. Objective measures however, rely on participants' performance in a forced choice task, where they typically have to choose between a stimulus that previously had been presented and a new distracter stimulus. If performance in such a task is at chance level, they concluded that the stimulus had been presented below the objective threshold of awareness.

Asking, whether conscious awareness had been involved or not is obviously not an option to study memory in preverbal human infants or in animals. Therefore, researchers with these interests had to rely more on the second crucial question distinguishing between declarative and nondeclarative memory: Is performance in a memory task dependent upon intact MTL structures? If animals with MTL lesions showed severely impaired performance in a specific memory task, it was concluded that the task measures a form of declarative memory. Researchers studying memory in young infants used a similar line of argumentation. They concluded that a task measured declarative forms of memory, if amnesic patients (or lesioned animals) failed to show normal performance in a parallel version of the task. This has for example been demonstrated for the "deferred imitation task", in which participants are shown a sequence of different events or target actions on novel objects, typically including 2 to 5 different events (e.g. a doll is undressed, put in a bath tube, dried, and re-clothed). After a determined delay, participants are presented with the objects again without any explicit instruction. The measure for the recall performance is how many target actions are recalled in the correct sequence (Bauer, 2002). McDonough and colleagues (1995) have shown that amnesic patients failed to reproduce modelled event sequences after a delay of 24 hours. Based on this finding they concluded that the "deferred imitation task" is appropriate to measure declarative memory.

However, the study presented here as well as several other recent studies reporting involvement of the hippocampal formation (Henke et al., 2003b; Henke et al., 2003a; Schendan et al., 2003) or in the perirhinal cortex (Rose et al., 2002) in implicit tasks in healthy participants question the validity of such conclusions. These findings lead to the hypothesis that involvement of MTL structures might be a prerequisite for declarative or explicit memory, but activation of MTL structures is not sufficient to induce conscious memory processes. Thus, the only clearly distinguishing feature between declarative and nondeclarative forms of memory on a neural level, i.e. the

hypothesis that MTL structures are exclusively involved in declarative memory is heavily questioned by these findings.

Distinguishing between declarative or explicit and nondeclarative or implicit forms of memory still might be reasonable to refer to memory contents we can consciously access compared to memory contents we can not. However, the level of awareness seems not to be a critical feature concerning the description of the neural network involved in performing a certain memory task. The neural network involved in a certain memory task seems rather to depend on the processing demands of the task than on the level of awareness. As the processing demands of commonly used tasks to measure nondeclarative memory are in general quite different from the processing demands of commonly used tasks to study declarative memory, some of the dissociations between the two forms of memory might have been induced by other task differences than the different level of awareness. One important difference is that declarative memory tasks typically require the ability to form new, flexible relations, an ability that is generally not required in classical nondeclarative memory tasks. All the authors that have observed activation of MTL structures in implicit memory tasks have used implicit tasks that required the formation of new relations (Henke et al., 2003a, 2003b; Rose et al., 2002; Schendan et al., 2003). As the main task of the hippocampal formation is assumed to be the formation of new, flexible relations (Cohen et al., 1999), the question of whether the hippocampus is involved or not might rather depend on the question, whether the task requires the formation of new relations than on the level of awareness.

Assuming that the recent findings will hold true, the declarative/nondeclarative account is no longer able to explain all findings from studies investigating specific forms of long-term memory, dissociations between different forms of long-term memory, or interactions between different forms of long-term memory. Therefore, it might be time to abandon declarative/nondeclarative or implicit/explicit accounts in favour of an account that has the power to explain the current findings better.

6.3 On the search of a model for long-term memory

6.3.1 The declarative/nondeclarative account revised – a poor solution

As discussed, hippocampus-dependent memory seems to be rather defined by the processing demands of the task than by the level of awareness. This implies that the functional distinction between declarative, i.e. memory with conscious awareness and nondeclarative, i.e. memory without conscious awareness may not be mirrored on a neural level in distinct underlying neural networks. As this is one of the core assumptions of the declarative/nondeclarative account, this account seems to capture rather poorly the properties and underlying neural structures of different forms of long-term memory. Therefore, the declarative/nondeclarative account should be adapted according to the recent findings, or abandoned in favour of a model that provides better explanations for the current status of knowledge.

A revised version of the declarative/nondeclarative account could for example keep the distinction between hippocampus-dependent and hippocampus-independent forms of memory on the neural level but adapt the definition of the functional properties according to the recent findings. As discussed earlier, the relational account seems to provide satisfying explanations for all current findings about hippocampus-dependent forms of long-term memory. According to the relational account the hippocampus is involved whenever a task requires the formation of new, flexible relations between different parts of an event with or without conscious awareness. Therefore, replacing the terms "declarative memory" and nondeclarative" by the terms "relational memory" and "non-relational memory" might be a better solution to distinguish between hippocampus-dependent and hippocampus-independent forms of memory.

However, a persistent weakness of dichotomous models based on the distinction between hippocampus-dependent and hippocampus-independent forms of memory is the inhomogeneity of hippocampus-independent forms of memory. Whereas hippocampus-dependent forms of memory are assumed to rely on one quite-well defined neural network, different neural networks are suggested to underlie the numerous functionally distinct forms of memory that are hippocampus-independent (Gabrieli, 1998; Schacter and Buckner, 1998; Squire, 1992a). These different neural networks are unified solely by the shared absence of dependency from the

hippocampus. As discussed earlier, the inhomogeneity of hippocampus-independent (referred to as nondeclarative) forms of memory is also reflected on a functional level. On a functional level, many very different forms of learning and memory such as priming, skill learning or conditioning are unified based on the rather rigid, inflexible nature of such memories and several researchers have criticised the "grab-bag-nature" of hippocampus-independent forms of memory (Rovee-Collier et al., 2000a).

Evidence for the distinction between hippocampus-dependent and hippocampus-independent forms of memory came from studies with amnesic patients. Hippocampal damage led to severe impairment in certain memory tasks, whereas other forms of learning and memory remained intact (Cohen and Squire, 1980; Corkin, 1968; Milner et al., 1968; Warrington and Weiskrantz, 1968). Initially, it was hypothesised, that amnesic patients perform poorly in tasks that require conscious awareness for the learning episode and the learning material, whereas they show normal learning and memory in tasks that are independent from conscious awareness for the learning episode or the learning material. Doubtlessly, the subjectively perceived quality of memories we can consciously access differs enormously from the quality of memories we can not consciously access. With regard to this aspect, the declarative/nondeclarative account was (and still is) convincing. The beauty of this account was that the distinction between declarative and nondeclarative memory seemed to be mirrored in distinct underlying neural networks. However, now as increasing evidence suggests that MTL structures, including the hippocampus, are also involved in certain implicit memory tasks, it has to be reconsidered whether the distinction between hippocampus-dependent and hippocampus-independent forms of memory is still appropriate. Whereas it is widely accepted that one single mechanism underlies hippocampus-dependent learning, it is still a matter of debate whether nondeclarative (or procedural) memory depends on one common learning mechanism as well. On a functional level, hippocampus-dependent learning is hypothesised to be fast (i.e. can happen in a single encounter) and to lead to flexible relations, whereas a common, slow, error-driven mechanism that leads to rather rigid associations is suggested to underlie hippocampus-independent learning (Gupta and Cohen, 2002; Norman and O'Reilly, 2003; O'Reilly and Rudy, 2000; Rolls and Treves, 1998). However, on a neural level nondeclarative forms of learning and memory are unified solely based on the shared absence of dependency of the hippocampus. The cost of a dichotomous model is therefore that it

always will poorly reflect the neural networks underlying the different forms of non-declarative learning and memory. Thus, a dichotomous model will never appropriately account for the variety of different forms of long-term memory on a neural level.

6.3.2 A potent(ial) alternative: Transfer appropriate processing (TAP)

The TAP account (Roediger et al., 1999; Roediger et al., 2002; Roediger et al., 1989b) offers an alternative to dichotomous accounts such as the declarative/nondeclarative or the implicit/explicit memory account. In the TAP account memory-encoding is conceptualised as the processes underlying perception and comprehension and retrieval as the logical consequence of encoding. Hence, retrieval tasks benefit from encoding to the extent that the processes required during retrieval overlap with the operations that were required during encoding, i.e. retention is determined by how well the processing requirements of the test matched those used originally to encode information. The TAP framework developed by Roediger and colleagues (1989b) widely neglected the investigation of brain structures underlying different processing modes. However, as the authors claimed themselves,

"(…) we must admit that there is no inherent reason that an approach specifying both memory systems and something like processing modes or procedures cannot be partially correct. Neural structures require processing for their operation, and procedures must be carried out by the brain." (Roediger et al., 1989b, p. 36)

All cognitive performance is a result of the processes performed by underlying neural systems. However, procedural frameworks such as the TAP account claim that neurocognitive systems are complex and interact on numerous levels and do not function as independent, encapsulated systems (Roediger et al., 2002). Moscovitch (1992) and Roediger and colleagues (1999) have proposed a more elaborated version of the TAP framework, a component-processing approach, suggesting, that any task can be conceptualised as a concatenation of component processes that depend on local neural networks. It seems very plausible then, that changing the task requirements will probably add or subtract one (or more) components. If different process components are involved in two different tasks, it can easily be imagined that this can produce dissociations that can be observed on a behavioural level. Furthermore, changing the process components will also change the involved neural networks. According to this view, it can be expected that numerous different memory

systems can be dissociated experimentally depending on the processing demands required to perform a specific task (for a summary see Roediger et al., 2002).

Concerning the neural networks underlying different learning and memory tasks, the TAP account would predict that the neural networks involved in learning and retrieval task overlap to the extent that the processing demands of the learning and the retrieval task overlap. Indeed, findings from imaging studies with fMRI or PET have provided evidence supporting this view (e.g. Moscovitch et al., 1995; Nyberg et al., 2000; Wheeler et al., 2000; Vaidya et al., 2002)

Wheeler and colleagues (2000) have reported evidence that the retrieval of vivid visual and auditory information can be associated with a reactivation of some of the same sensory regions that were activated during perception of those items. In their study, participants encoded a set of pictures or sounds referring to identical items. Each item was paired with a descriptive label, i.e. the label DOG was paired with a picture of a dog for one half of the participants or with the sound of a dog barking for the other half. After encoding, event-related fMRI signal changes were investigated with three different tasks. In the recall task, participants saw only the labels of previously studied items. They were instructed to actively retrieve the pictures or sounds from long-term memory and to indicate, whether the label had been presented in combination with a sound or with a picture. During the perception task, the studied sounds and pictures (old) were presented and participants indicated again, whether the items were sounds or pictures. A third task was used, that was identical to the perception task with the exception that the presented items had not been studied previously (new). During the retrieval of the pictures, i.e. vivid visual information, Wheeler and colleagues (2000) observed activations in secondary visual areas, such as an area in the left fusiform region and bilateral dorsal regions near precuneus. In contrast, the retrieval of sounds, i.e. vivid auditory content, activated secondary auditory areas. The authors concluded that retrieval of sounds and pictures activates a subset of those sensory-specific areas involved in perception, particularly late rather than early sensory regions.

A very similar experiment had been carried out by Nyberg and colleagues (2000) using PET. In their study, two different encoding tasks were used. In one task participants encoded visual words that were combined with complex sounds whereas they encoded visual words only in the second task. Each encoding task was followed

by a retrieval task. Participants were instructed to indicate for each item (1) whether they recognised it and remembered that it had been paired with a sound at study (2) whether they recognised it and remembered that it had been presented alone at study, or (3) whether they thought it was new. Only the retrieval of the words that had been presented in combination with a sound was expected to induce retrieval of auditory event information. Indeed, their results support the hypothesis that remembering, that a word had been paired with a sound during encoding, results in an activation of auditory cortex.

Moscovitch and colleagues (1995) have reported data indicating that distinct neural correlates underly memory for spatial location and memory for object identity of the very same stimuli. Participants studied a set of displays consisting of three unique line drawings that were arranged in different spatial configurations. Memory for spatial location and for object identity was tested with a retrieval task. Participants were presented with pairs of displays and had to indicate which one was new and which one had been studied previously. New displays were obtained by either changing the spatial configuration (spatial retrieval task) or the identity of one of the objects (object retrieval task) of a studied display. A perceptual baseline task was included to assure that any observed differences between the spatial and the object retrieval are rather related to retrieval from long-term memory than to any differences in perceptual, attentional, or working memory processes. Whereas retrieval of spatial location activated brain regions that are also associated with perception of spatial location (inferior parietal lobule, part of the dorsal visual pathway) the retrieval of object identity activated regions that are also associated with processing of information about object identity (inferotemporal cortex, part of theventral visual pathway).

Although the network of retrieval and encoding had not been directly compared in our present study (chapter 5) and in previous studies of Henke and colleagues (2003a, 2003b), we observed that very similar networks were engaged during encoding and retrieval of face-profession associations. The networks included for example an area in the fusiform gyrus that is suggested to be crucially involved in face-processing and areas suggested to be critically involved in semantic word processing located in the temporal lobes and inferior frontal brain regions. Moreover, we observed similar networks engaged in implicit and explicit encoding and retrieval of face-profession associations.

Taken together, these results suggest that retrieval of LTM is a multicomponent process. These studies support the hypothesis that the network underlying the retrieval process is closely related to the network initially involved in perception and identification of those events. Hence, these results are in full agreement with component-processing accounts (Moscovitch, 1992; Roediger et al., 1999; Roediger et al., 2002).

Moreover, the heterogeneity of the distinct neural networks underlying different forms of learning and memory such as priming, skill learning or conditioning is not difficult to explain with TAP or component-processing accounts. Given that distinct neural networks underlie functionally different learning and memory tasks depending on the processing demands of a certain tasks it is a logical consequence that tasks requiring motor learning and retrieval involve the proper functioning of motor areas and the cerebellum (Gabrieli, 1998), but visual priming depends on visual cortices, whereas conceptual priming depends more on brain areas involved in semantic processing (Schacter and Buckner, 1998).

The results we have reported in our study and other studies are evidence, that different neural networks might be at work simultaneously enabling complex interactions between different systems devoted to different processing aspects (Eichenbaum et al., 1988; Poldrack et al., 1999, 2001). These observations are additional support for the hypothesis that events are processed by distinct neural networks according to their capabilities in parallel and are in full agreement with processing accounts like TAP or component-processing account.

TAP or component-processing accounts seem to provide better and more parsimonious explanations for the current status of knowledge about different aspects of long-term memory. Relational or hippocampus-dependent memory can be integrated as one system with fairly well-defined processing components.

6.3.3 Integrating systems accounts and component processing accounts

The various aspects currently known about long-term memory might be explained best by a model that integrates aspects of models suggesting different memory system and component processing accounts. As already noted, the component-

processing account was championed by Moscovitch (1992). He proposed a model involving four essential components:

1) a non-frontal neocortical component consisting of perceptual and interpretative semantic input modules that mediate performance on item-specific, implicit tests of memory such as priming,
2) a medial temporal/hippocampal component mediating associative memory, i.e. encoding, storage and retrieval on explicit, episodic tests,
3) a frontal-lobe component working as central system that integrates information of the other components and hence mediates performance on strategic explicit tests and on rule-bound implicit tests such as cognitive skill learning,
4) a basal ganglia component that mediates performance on sensorimotor, procedural tests of memory.

Moscovitch (1992) proposed that the medial temporal/hippocampal component is exclusively involved in explicit forms of memory in agreement with declarative/nondeclarative or explicit/implicit accounts. Moreover, he assumed that memory is a natural consequence of apprehending the material *consciously*.

Clearly, the role of the medial temporal/hippocampal component has to be redefined according to the results reported in the present study (chapter 5) and further recent findings suggesting a role of the hippocampus also in implicit relational memory (Greene et al., 2001; Henke et al., 2003a, 2003b; Rose et al., 2002; Schendan et al., 2003). Based on these findings it can be concluded that involvement of the medial temporal/hippocampal component is not dependent on conscious apprehension of the learning material. The functioning of the medial temporal/hippocampal system could be redefined according to the relational account (Cohen et al., 1999). The relational account claims that the hippocampus is engaged in the formation of flexible relations between unrelated parts of an episode, irrespective of the level of awareness. With this hypothesis, the relational account offers satisfying explanations for all current findings concerning hippocampus-dependent memory.

Further aspects of Moscovitch (1992) concerning the function of the medial temporal/hippocampal component such as the assumption that the hippocampus-dependent memory system encodes and stores information automatically can clearly be integrated into the relational account. Moscovitch (1992) assumed that

advantages of an automatic hippocampal component are, that it does not draw cognitive resources away from other activities, and that memory does not rely on our intentions to remember, which is important because we rarely know in advance what will be worth to be remembered later.

Moscovitch (1992) does not conceptualise the four mentioned components as functioning independently from each other, but emphasizes the importance of the interrelatedness of the various components as follows:

"The components function is determined not only by their internal organization but also by the network of connections to other components. The interrelatedness of the various components that is specified in the model helps explain why memory tests (and memory in real life situations) are not likely to be process (or component)-pure when administered to people who are neurologically intact." (Moscovitch, 1992; p. 265)

Moscovitch (1992) conceptualises memory in his component process account as dependent on potentially independent, but typically interactive, components. According to this concept, memory is not divided into different subsystems.

However, the mentioned four components might also be conceptualised as critical structures that are parts of neural networks underlying functionally different memory systems, hence, integrating component process accounts and memory system models into a "systems processing account". The neural networks underlying the functionally different systems of long-term memory might be hypothesised to overlap and interact on multiple levels but to rely each on at least one critical structure that is not crucially involved in the other forms of long-term memory. According to processing accounts, the neural networks underlying a specific form of learning and retrieval will involve additional neural components according to the specific processing demands of a certain task. A memory task requiring participants to establish links between faces and words will for example include areas specifically involved in face processing, whereas a learning task requiring participants to establish links between sounds and words will probably involve areas relevant for sound processing but not areas involved in face-processing. Both tasks however, will include brain regions supporting word processing and brain regions that are involved in the formation of new links between unrelated items. Of course, these two tasks should not be conceptualised as two different memory systems, although the

underlying neural networks will not be identical. This example points to a risk the proposed "systems processing account" bares. Careful analysis of the processing demands of a certain memory task are necessary to reveal which aspects are primarily related to memory and which aspects are primarily relevant for other aspects of the task, such as stimulus processing. In the previous example the common aspect concerning memory that is required in both tasks would be the formation of a new association between previously unrelated items.

Such a view of long-term memory can perfectly explain interactions between different memory systems. A competitive interaction has for example been observed by Poldrack and colleagues (2001) between the memory system depending on the medial temporal/hippocampal component and the memory system depending on the basal-ganglia component (for a review see Poldrack and Packard, 2003). Following this line of argumentation, one might speculate that different memory systems interacted during implicit learning in the present study (chapter 5) leading to memory traces affecting later explicit memory encoding and leading to an impaired retrieval performance.

Based on findings of studies with different patient groups as well as dissociations between different forms of memory observed on a functional level in normal humans, a segregation between at least 5 functionally different memory systems that critically depend on different neural substrates could be proposed (Table 1).

The five different proposed memory systems are not new. Its functional properties and the underlying neural networks have been investigated in many experiments with humans and animals. The current knowledge about the characteristics of these systems had been described in chapter three in more detail (for a description of the properties of “Relational memory” see 3.5.2 The relational account; for a description of the other four memory systems see 3.2.2 Nondeclarative memory).

Table 1. A proposal for different memory systems.

Memory system	Functional Features	Critical neural structure
Relational memory	• fast, one trial • associative, relational • flexible • implicit and explicit	• hippocampus
Perceptual repetition priming	• fast • modality and material specific • implicit	• modality specific sensory neocortex
Conceptual repetition priming	• fast • not modality and material specific • implicit	• neocortical areas specific for semantic processing (inferior frontal areas, lateral temporal lobes)
Skill learning	• slow, error driven acquisition of (complex) rules and motor abilities • implicit	• basal ganglia
Classical conditioning	• slow, error driven acquisition of simple stimulus-response associations • implicit	• Cerebellum

In contrast to traditional models of memory systems, the five different memory systems are conceptualised as five equivalent systems in the proposed “systems processing account”. Traditional models of memory systems suggest a hierarchical structure of long term memory. On a first level, a distinction is made between memory systems depending on conscious awareness (declarative memory or explicit memory) and memory systems that do not (nondeclarative memory or implicit memory). On a second level it has been further distinguished between different forms of declarative (such as episodic and semantic) and nondeclarative (such as perceptual and conceptual priming, skill learning, and classical conditioning) forms of memory (e.g. Squire and Zola-Morgan 1988). This hierarchical structure seemed to be supported by evidence suggesting that the functional distinction is also mirrored on a neural level. It was assumed that only declarative forms of memory depend on MTL structures. However, as summarised in this thesis, increasing experimental evidence suggests a role of MTL structures also in implicit forms of memory (e.g.

Henke et al., 2003a, 2003b; McIntosh et al., 2003; Rose et al., 2002; Schendan et al., 2003), leading to the assumption that a differentiation between declarative and nondeclarative forms of memory is not mirrored on a neural level. Therefore, it seems appropriate to abandon models proposing a hierarchical structure of long term memory in favour of models suggesting that long term memory consists of several equivalent subsystems. Each subsystem can be defined by characteristic functional and neuroanatomical properties.

Relational memory seems to be the only form of learning that allows the rapid formation and later retrieval of new and flexible associations between previously unrelated items. It had been demonstrated that the rapid formation of multiple, semantic, spatial, or temporal associations corresponds to the computational expertise of the hippocampus and related cortices (e.g. Cohen and Eichenbaum, 1993; Davachi et al., 2003; Henke et al., 1997, 1999; Lepage et al., 2000; Mayes et al., 1998; Montaldi et al., 1998; Rolls and Treves, 1998; Small et al., 2001; Sperling et al., 2001; Wallenstein et al., 1998). This explains why MTL dependent memory, i.e. relational memory is of special interest for humans. Our every day life memories for autobiographical episodes (episodic memory) consist of numerous different pieces of semantic, temporal and spatial information. Moreover, episodes are effortlessly remembered. An episode that has been experienced once can usually be remembered without training or rehearsal. Thus, their nature is typically relational.

So far, it had been assumed that new associations can only be acquired slowly over a high number of trials in forms of learning and memory that do not depend on conscious awareness for the learning episode such as skill learning or classical conditioning (Norman and O'Reilly, 2003; O'Reilly and Rudy, 2000; Rolls and Treeves, 1998). Increasing evidence now suggests that rapid associative learning and retrieval may occur without conscious awareness and engages the hippocampus and parahippocampal gyrus (e.g. Henke et al., 2003a, 2003b; McIntosh et al., 2003; Rose et al., 2002; Schendan et al., 2003). This leads to the hypothesis that our everyday life memories might also be influenced by episodes we are not able to retrieve consciously.

To end, it is briefly explained why semantic memory, the memory for facts, is not included as additional memory system in the proposed "systems processing account". Semantic memory is conceptualised as a special form of relational or

episodic memory and not as an additional functionally and anatomically distinct form of memory. This is in line with the hypothesis that most memories that are stored for a very long time loose their episodic nature as time goes by and become more semantic and fact like over time (see also Rosenbaum et al. 2000). This process might involve that originally episodic memories loose most of the initially stored contextual information, i.e. less relational associations of an episode can be retrieved. The more time has gone by, the more likely the memory content gets semanticised, i.e. integrated into the neocortically represented semantic system and so can be retrieved independently from MTL structures.

7 Concluding remarks

Declarative/nondeclarative or explicit/implicit accounts should be abandoned for two reasons. First, increasing evidence suggests that the hippocampus is not exclusively involved in explicit memory tasks or declarative memory, but is engaged whenever a task requires the formation of new, flexible relations between previously unrelated items irrespective of the level of awareness. Second, a dichotomous model will never appropriately account for the variety of different forms of long-term memory on a neural level. A "systems processing account" is proposed as an alternative, integrating aspects of processing and systems accounts for long-term memory. Certainly, it is necessary to define the different neural networks as well as the functional differences between the proposed different forms of learning and memory more specifically. Experiments comparing directly the neural networks involved in different memory tasks varying systematically one specific component, such as input modality, might be useful in revealing neural substrates underlying more general aspects of the memory task. Furthermore, experiments addressing directly how different forms of learning and memory interact will clearly provide valuable evidence about the complex structure and functioning of long-term memory.

Only future research will reveal how appropriate the suggested "systems processing account" can model the different aspects of long-term memory at both the structural and the process level.

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9 Appendix

9.1 Behavioural data

9.1.1 Reaction times: Encoding task

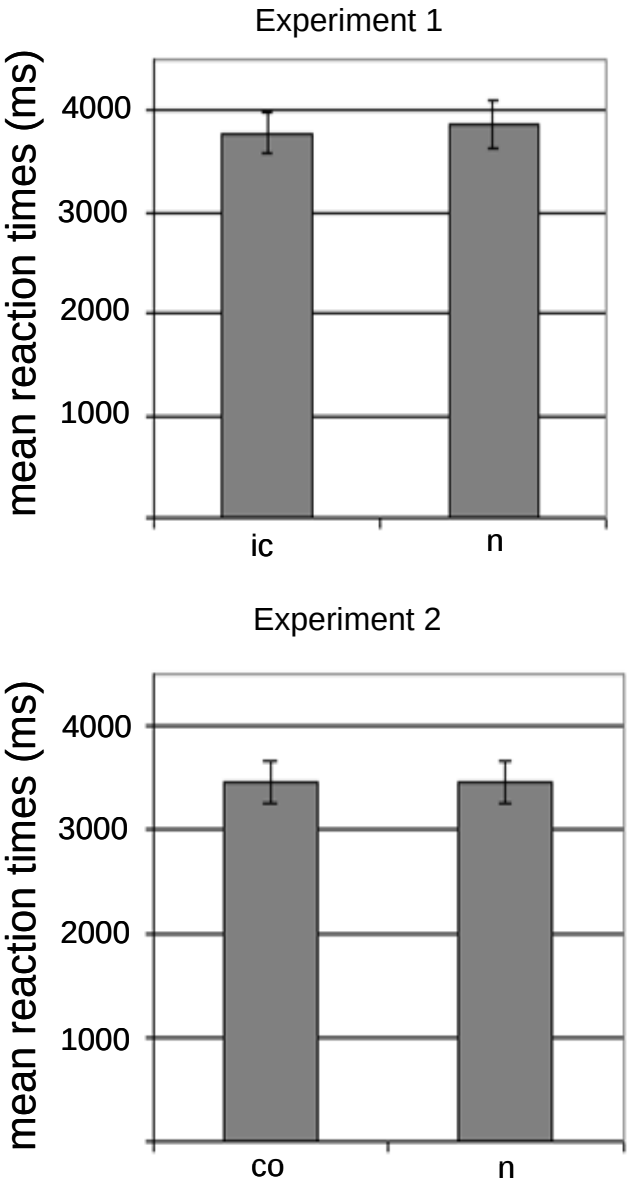

Figure A. Reaction time data of the encoding task (imagining a scene). The upper panel shows the mean reaction times and the SEM of the incongruent (M = 3780.9, SEM = 195.8) and the neutral condition (M = 3859.0, SEM = 238.5) of experiment 1. The lower panel shows the mean reaction times and the SEM of the congruent (M = 3449.3, SEM = 212.7) and neutral condition (M = 3450.3, SEM = 201.2) of experiment 2. Separate t-tests for each experiment revealed no significant differences in mean reaction times between the conditions neither for experiment 1 ($t(15) = -0.46$, $p = 0.653$) nor for experiment 2 ($t(12) = -0.01$, $p = 0.99$).

9.1.2 Reaction times: Retrieval task – correct vs wrong answers

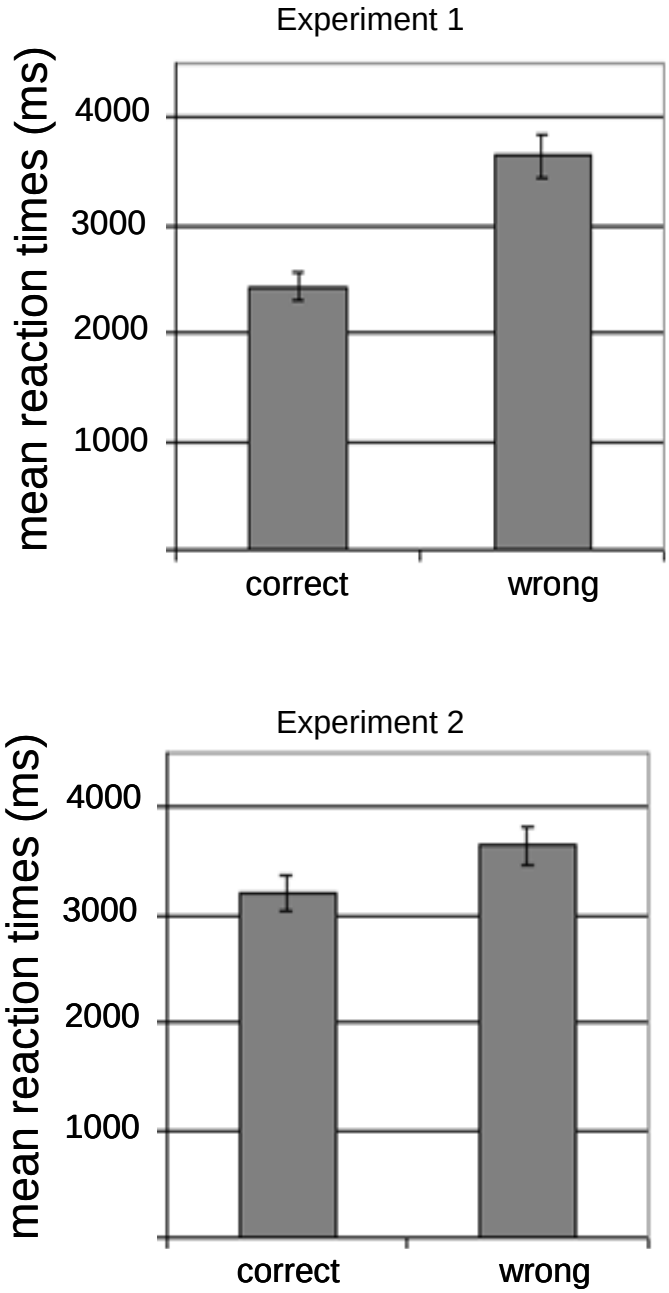

Figure B. Comparison between reaction times for correct and wrong answers of the retrieval task. The task instruction was to retrieve the professional word and indicate the professional category. The upper panel shows the mean reaction times and the SEM for correct (M = 2435.1, SEM = 123.2) and wrong answers (M = 3643.4, SEM = 196.5) in experiment 1 (incongruent). The lower panel shows the mean reaction times and the SEM for correct (M = 3206.4, SEM = 174.9) and wrong answers (M = 3640.1, SEM = 176.6) of experiment 2 (congruent). Reaction times for correct answers were significantly faster for correct than for wrong answers in both experiments (experiment 1: (t(15) = -6.80, p = 0.000; experiment 2 (t(14)= -2.96, p = 0.01)).

9.1.3 Reaction times: Retrieval task – comparison between conditions

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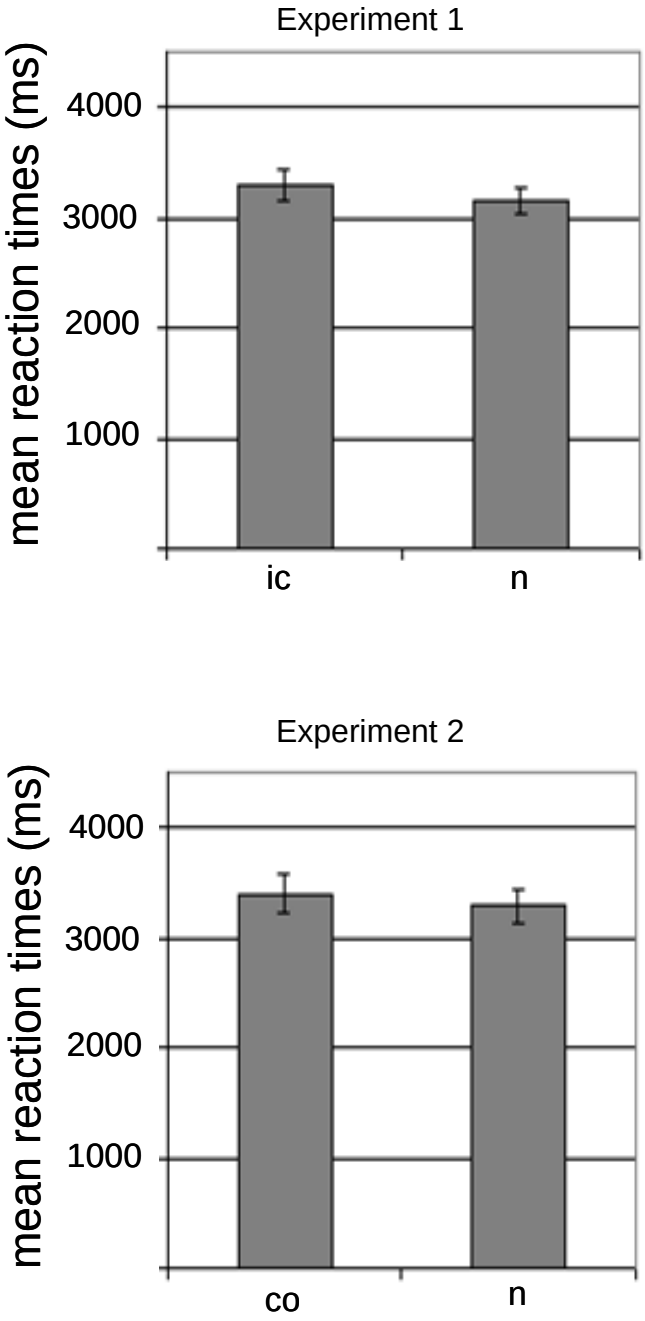


Figure C. Reaction times are compared between the experimental conditions of the retrieval task. The left panel shows the mean reaction times and the SEM of the incongruent (M = 3307.1, SEM = 138.3) and the neutral condition (M = 3164.5, SEM = 113.5) of experiment 1. The right panel shows the mean reaction times and the SEM of the congruent (M = 3405.4, SEM = 179.1) and the neutral condition (M = 3284.8, SEM = 174.9) of experiment 2. Separate t-tests for each experiment revealed no significant differences in mean reaction times between the conditions neither for experiment 1 ($t(15) = 1.15$, $p = 0.27$) nor for experiment 2 ($t(14) = 1.18$, $p = 0.26$).

9.2 Imaging data

9.2.1 Functional T2*-weighted image

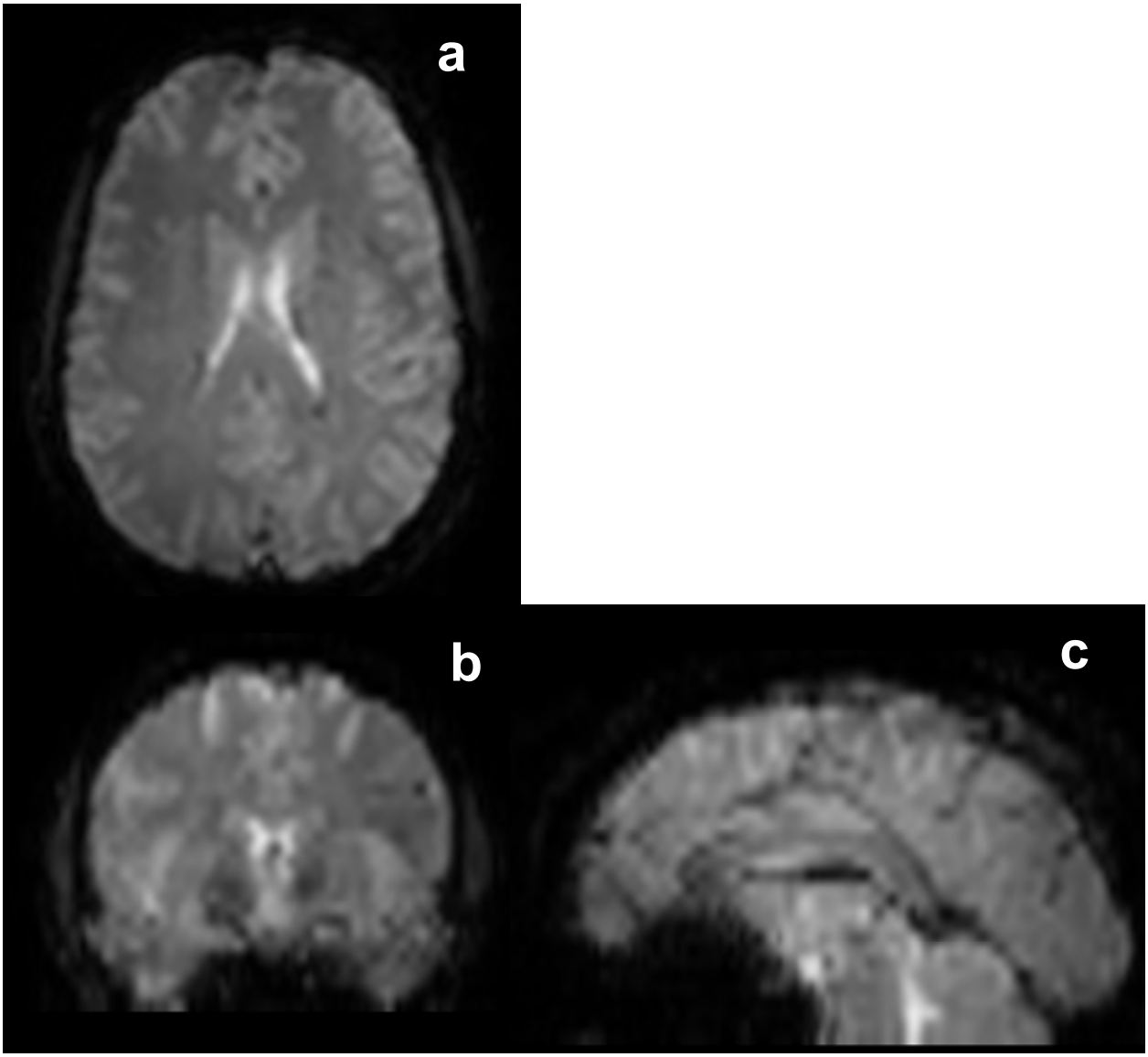
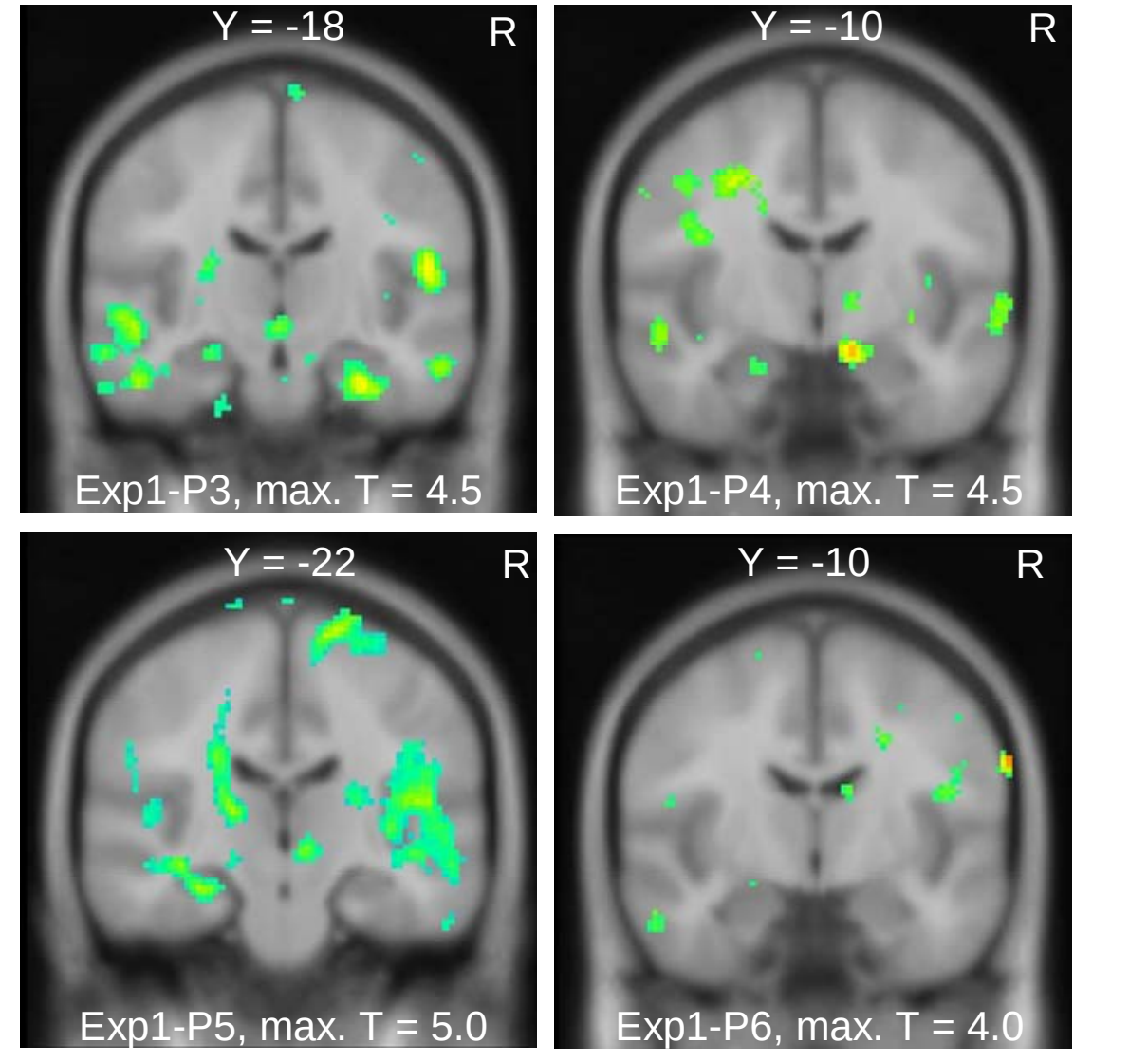
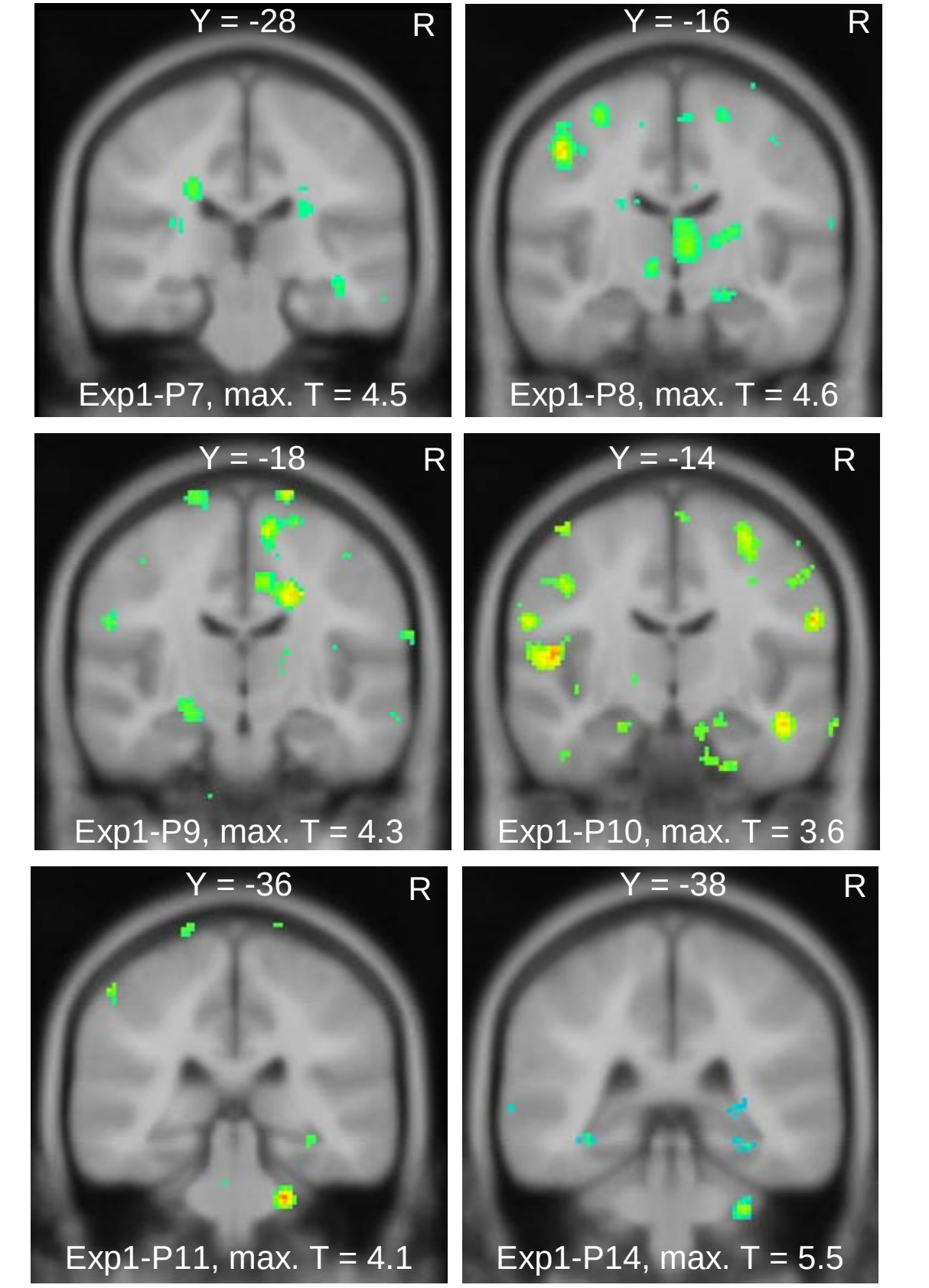


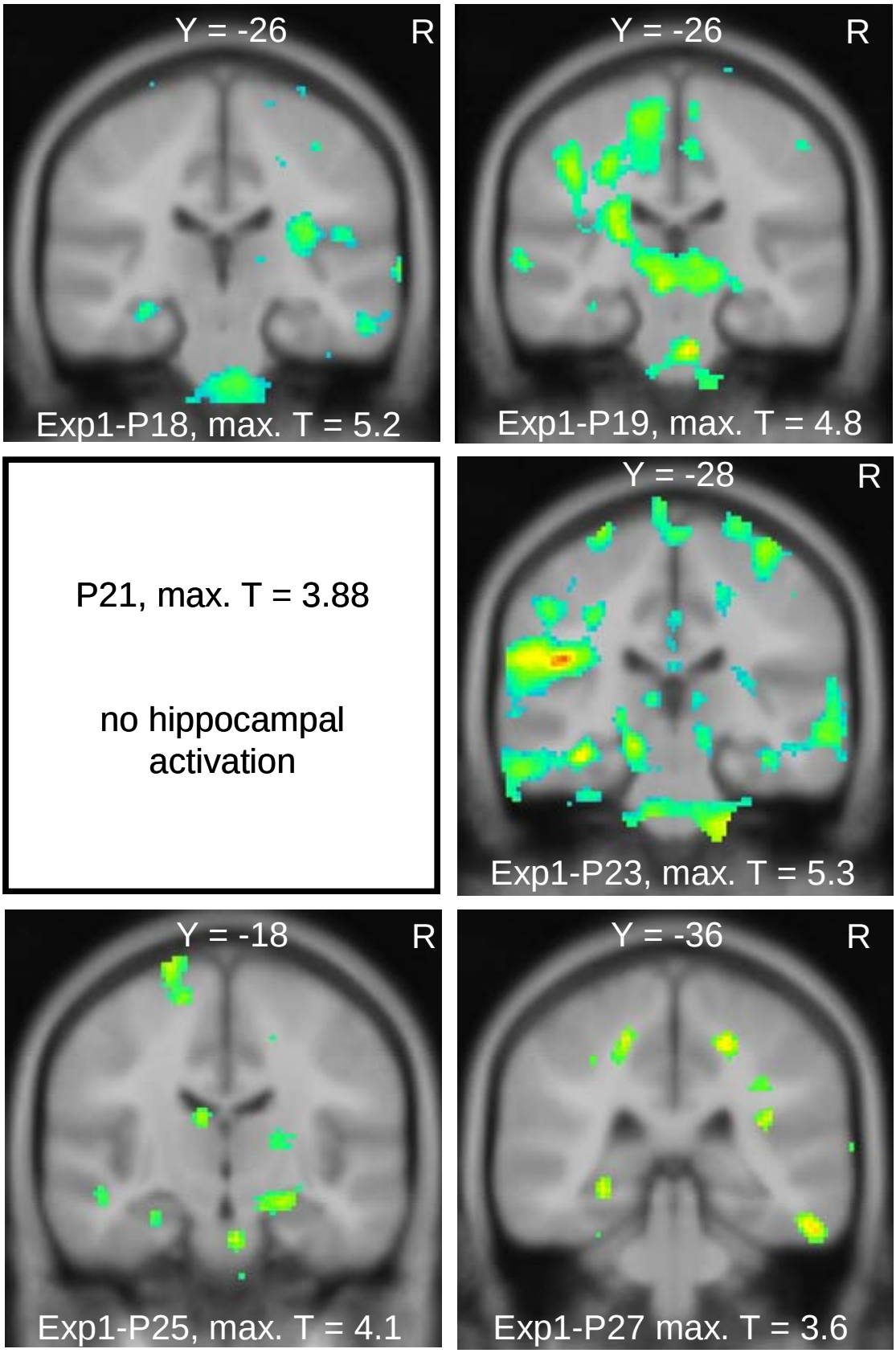
Figure D. Example of a raw functional T2* weighted MR image of one of our participants. (a) axial view, (b) coronal view, and (c) sagittal view .

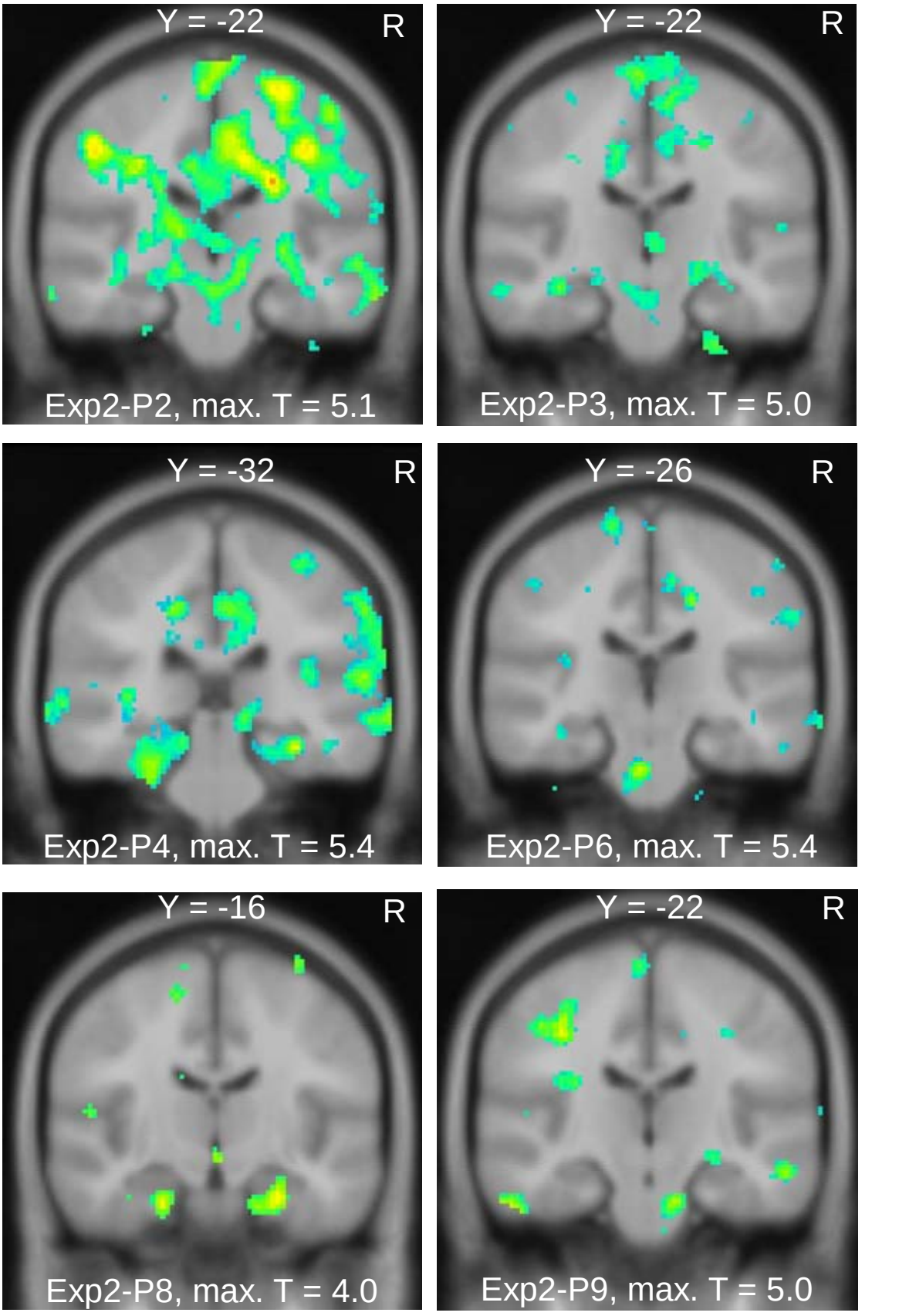
9.2.2 MTL activations during implicit encoding – single subjects

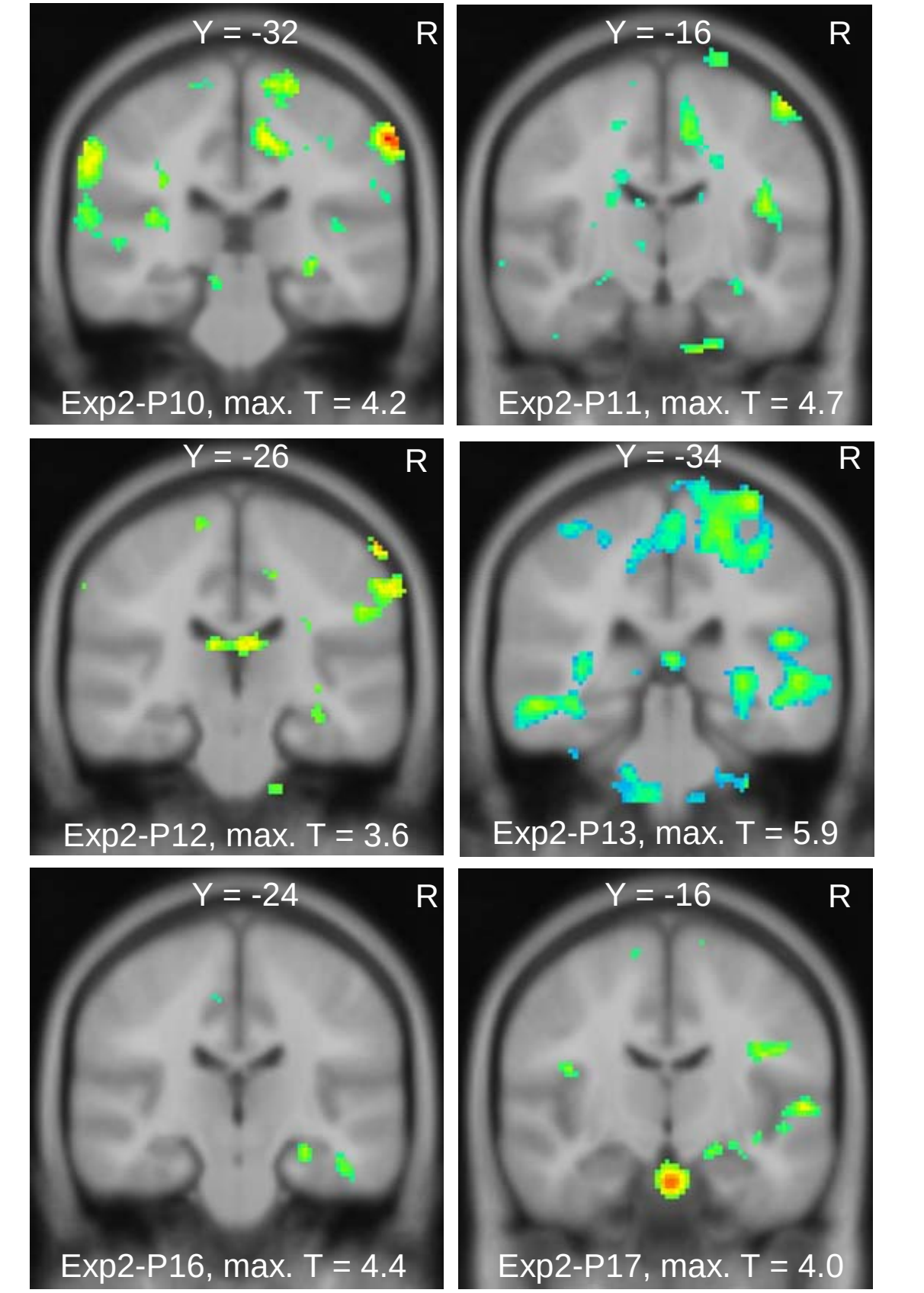
Figure E. MTL activations for individual subjects are shown on p. 134 –138. Brain activity underlying implicit word reading and the implicit formation of semantic face-profession associations was revealed by comparing the masked presentation of face-profession pairs (incongruent or congruent condition) to the masked presentation of face-nonword pairs (neutral condition) in each participant. The location of peaks of significant BOLD signal changes are shown as colour coded t-values superimposed on coronal slices of the T1-weighted MNI-template provided in SPM2. The location of the coronal slice is indicated by MNI y-coordinates. Data in this illustration are thresholded on $p < 0.05$.




Y = -28
R
Exp1-P7, max. T = 4.5
Y = -16
R
Exp1-P8, max. T = 4.6
Y = -18
R
Exp1-P9, max. T = 4.3
Y = -14
R
Exp1-P10, max. T = 3.6
Y = -36
R
Exp1-P11, max. T = 4.1
Y = -38
R
Exp1-P14, max. T = 5.5
0.0
max. T


Y = -26
R
Exp1-P18, max. T = 5.2
Y = -26
R
Exp1-P19, max. T = 4.8
P21, max. T = 3.88
no hippocampal activation
Y = -28
R
Exp1-P23, max. T = 5.3
Y = -18
R
Exp1-P25, max. T = 4.1
Y = -36
R
Exp1-P27 max. T = 3.6
0.0
max. T


Y = -22
R
Exp2-P2, max. T = 5.1
Y = -22
R
Exp2-P3, max. T = 5.0
Y = -32
R
Exp2-P4, max. T = 5.4
Y = -26
R
Exp2-P6, max. T = 5.4
Y = -16
R
Exp2-P8, max. T = 4.0
Y = -22
R
Exp2-P9, max. T = 5.0
0.0
max. T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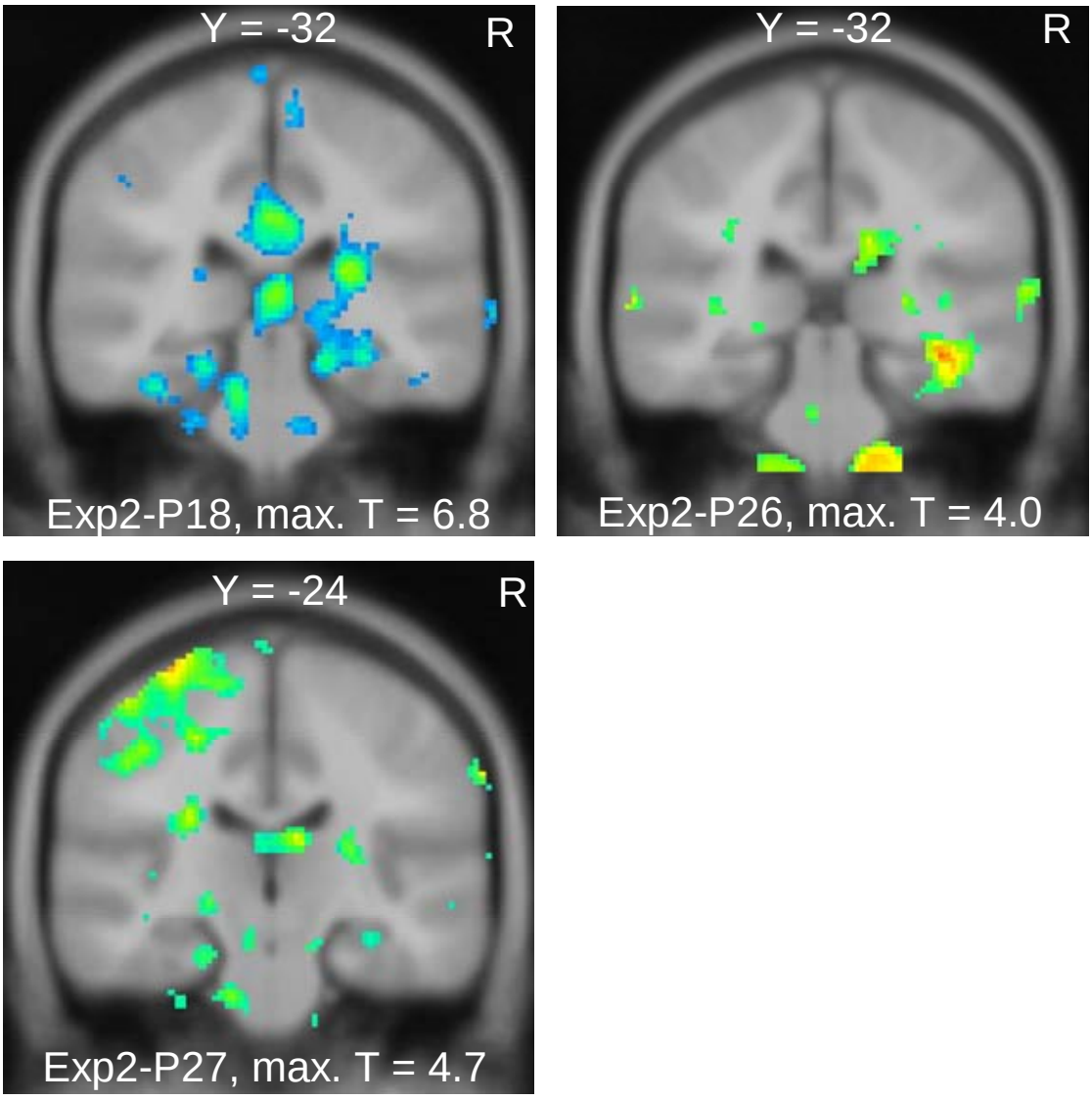
R
Exp2-P10, max. T = 4.2
Y = -16
R
Exp2-P11, max. T = 4.7
Y = -26
R
Exp2-P12, max. T = 3.6
Y = -34
R
Exp2-P13, max. T = 5.9
Y = -24
R
Exp2-P16, max. T = 4.4
Y = -16
R
Exp2-P17, max. T = 4.0
0.0
max. T


Y = -32
R
Exp2-P18, max. T = 6.8
Y = -32
R
Exp2-P26, max. T = 4.0
Y = -24
R
Exp2-P27, max. T = 4.7
0.0
max. T

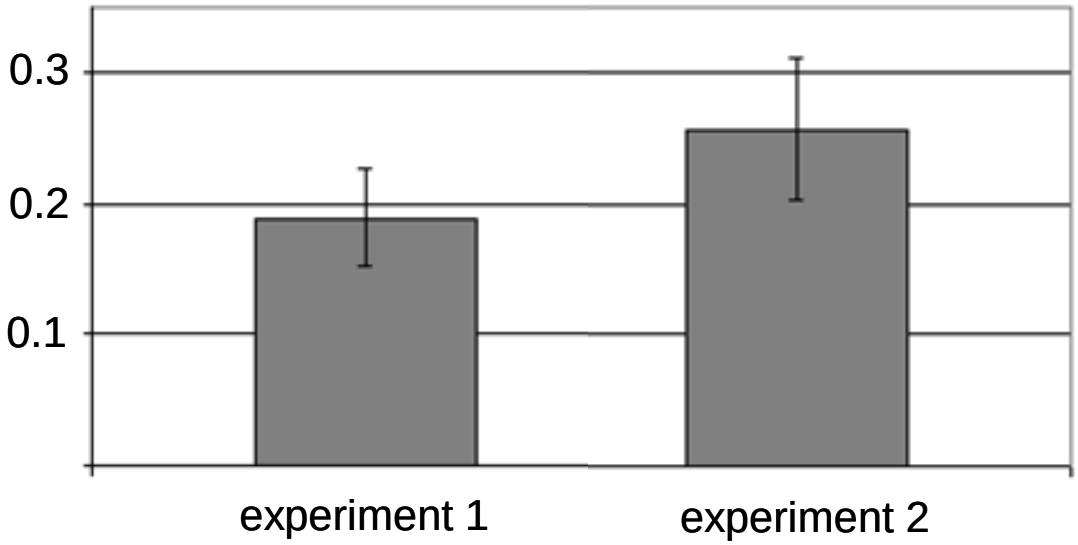


Figure F. Magnitude and variance of signal change in the hippocampus during implicit learning. The group mean and the SEM of the signal change is shown for the coordinate of the voxel with the highest T-value in the group analysis revealing activations underlying implicit encoding (one sample t-test). The left panel shows the magnitude and the variance of the signal change for MNI coordinate position -28, -18, -12 (left hippocampus, T = 5.08) in experiment 1 (incongruent; M = 0.19, SEM = 0.03). The right panel: shows the magnitude and the variance of the signal change for MNI coordinate position 30, -22, -12 (right hippocampus, T = 4.82) in experiment 2 (congruent; M = 0.26, SEM = 0.05).

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